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CARCINOMA OF THE THYROID IN CHILDREN AFTER X-RAY THERAPY IN EARLY CHILDHOOD

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Carcinoma of the thyroid in children is being diagnosed with increasing frequency. Several explanations have been offered to help explain this. Among these is the formerly prevalent use of x-ray therapy for benign childhood conditions. If a carcinogenic mechanism is involved we should expect a decrease in the incidence of this neoplasm in the future, as the practice of using irradiation for benign conditions in children is being abandoned. Also, if such a mechanism exists, it probably operates most strongly during infancy. Thyroid cancer after irradiation in adults is a rarity. Of 357 children with reported thyroid carcinomas, approximately one-third had received prior radiation therapy to the pharynx, neck, or chest for nonmalignant conditions. Further studies are needed before definite conclusions are reached, and until that time children should be protected from ionizing radiation in the treatment of benign conditions.

IN 1950 Duffy and Fitzgerald[1] reported 28 cases of carcinoma of the thyroid gland in children under 18 years of age and found that 10 of them had received irradiation to the thymus in infancy. Hesitant to draw conclusions from this finding, they suggested that this association might be profitably explored. Since then 114 cases of thyroid cancer have been reported in children who have had previous x-ray therapy in early childhood to the thymus, neck, or head areas for benign conditions. Ten cases of carcinoma of the thyroid, in children 17 years old or younger, have been observed in the Atlanta, Ga., area. Seven of these 10 patients received x-ray therapy for benign conditions in infancy or in early childhood. The purpose of this report is twofold: (1) to add these seven cases to the previously reported instances of thyroid neoplasia in children after irradiation and (2) to discuss the relationship between x-ray therapy and subsequent carcinoma of the thyroid.

Etiological Considerations

Carcinoma of the thyroid in children is being diagnosed with increasing frequency. This increase has been repeatedly stressed by Winship[2] and

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graphically demonstrated by Clark[3] in a convincing manner. Several explanations have been offered. First, some of these tumors may have gone unrecognized and untreated in the past and possibly the patients involved have reached adulthood before the condition is diagnosed. Perhaps some cases are being diagnosed earlier today since patients and physicians have been made more aware of the dangers of neglecting a persistently enlarged nodule.

This may explain some of the cases in the older children but would not seem to account for the over-all growing incidence in recent years. A second possibility is that an enlarged thymus in infants is in some manner related to the subsequent development of thyroid cancer. This, too, would not seem likely, since the so-called enlarged thymus in infancy is rather common and the occurrence of thyroid cancer during childhood is rather uncommon. No clinical or experimental proof has yet been offered to support this possibility. Also, we and other workers, such as Clark,[3] have seen thyroid cancer after x-ray therapy to the head or neck in children with apparently normal thymus glands. A third possibility to be considered is that the widespread use of x-ray therapy in infancy, during the same period when the rate of thyroid cancer in children was growing, is in some manner related to the subsequent thyroid neoplasia.

TABLE 1.—*Summary of Reported Cases of Thyroid Carcinoma in Children After Irradiation*

Author	Year Reported	Cases, No.
Quimby and Werner[5]	1949	1
Duffy and Fitzgerald[1]	1950	10
Warren, S., and others: Cancer 6:1139, 1953	1953	1
Clark[3]	1955	15
Buckwalter, J. A : J. Clin. Endocrinol. 15:1437, 1955. Buckwalter, J. A., and Meredith, L. K.: Pediatrics 15:317, 1955	1955	9
Uhlmann, E. M.: J A. M. A. 161: 504-507 (June 9) 1956	1956	4
Majarakis, J. D., and others: J. Clin. Endocrinol. 16:1487, 1956	1956	10
Fetterman, G. H.: A. M. A. J. Dis. Child. 92:581, 1956	1956	8
Winship[9]	1956	27
Simpson and Hempelmann[7]	1957	11
Cohen, E. A., and Hyman, C.: Am. Surgeon 23:240, 1957	1957	1
Wilson, H., and Asper, S., quoted by Duffy.[6]	...	17
Present study	1958	7
Total		121

Irradiation to the thymus gland in infancy was apparently popularized by Friedlander[4] in 1907 for what was termed "status-thymolymphaticus." X-ray therapy for the "enlarged thymus gland" was widely accepted and widely practiced from about 1930 to about 1950 and is still in vogue in some areas. Reasons quoted for irradiating the thymus include "routine x-ray therapy for enlarged thymic shadow," "referring physician requests x-ray therapy," "hiccoughs," "cough," "regurgitation after feedings," and many other frequently encountered minor problems in infancy.

Radiation to enlarged lymphoid struc oropharynx, to persistently enlarged cervical ly phatics, and to the chest for chronic cough were also accepted procedures during this same period. The diagnosis of thymic enlargement is not entirely satisfactory, since normal limits of mediastinal measurements in infants are not well established and they vary considerably depending on respiratory phase, cardiac phase, and position of the patient. Many cases of so-called enlarged thymus diagnosed from a chest roentgenogram are found to be caused by the film being exposed during the expiratory phase. In these cases, the "enlarged thymus" will disappear when a good inspiratory roentgenogram is taken. Prominent thymus glands are frequently encountered in asymptomatic infants. Most radiologists and pediatricians now believe that the thymus seldom, if ever, produces respiratory embarrassment or any other symptoms.

Rarity of Thyroid Neoplasia After Radiation in Adults

Several authors have looked with interest on the association between the widespread use of x-ray therapy in early childhood and the increased incidence of thyroid cancer in childhood during the same period. Let us examine this relationship more closely. There is a paucity of reports dealing with thyroid neoplasia after irradiation in adults. There have been no reports of thyroid carcinoma after x-ray therapy for laryngeal carcinoma, even though the thyroid receives many times the dose used to irradiate a child's thymus. There have been no reports of thyroid cancer developing in patients treated with radioactive iodine. In response to a questionnaire sent to 70 radiologists and 31 thyroid specialists, Quimby and Werner[5] found 10 cases of thyroid cancer which followed x-ray therapy for hyperthyroidism and stated that in only 3 of these did they think that the irradiation might be implicated in the production of the thyroid neoplasms. Three hundred twenty-eight patients with thyrotoxicosis treated by x-ray therapy were recently studied by Duffy[6] 25 years after their therapy, and no evidence of thyroid cancer was found in these patients.

In contrast to the paucity of reports dealing with this problem in adults, 114 cases of thyroid cancer have been reported in children who have received x-ray therapy in early childhood. These, plus our seven cases, are summarized in table 1. These statements lend support to the opinion of others who feel that, if there is a carcinogenic mechanism involved, it probably operates most strongly when radiation is given during infancy or early childhood.

The study of Simpson and Hempelmann,[7] was especially interesting, since they attacked this relationship in a different manner than that of most of the other reports. They obtained follow-up information on 1,052 of 1,722 children who received thymic radiation during the preceding 27 years and also obtained information on 1,933 siblings of these children who received no x-ray therapy. Eleven children in the treated group developed carcinoma of the thyroid, while none of their untreated siblings developed this neoplasm. The authors state that the number of cases of thyroid carcinoma is significantly higher in the treated group compared with their untreated siblings and with the general population. They also stated that the incidence of leukemia was significantly increased in the group receiving irradiation. The relationship between radiation and leukemia is outside the scope of this report but is adequately discussed by Lewis.[8] Winship[9] states that there was a history of x-ray therapy to the thymus during infancy in approximately 20% of the 334 cases of thyroid cancer during childhood that he collected. When radiation for other benign childhood conditions about the chest, neck, and head is added, it may raise the figure still higher. Clark[3] reported on 15 children with thyroid carcinoma and found not only that thymic irradiation was associated with subsequent thyroid cancer but that irradiation for other benign childhood conditions might also be involved. Only 4 of his 15 patients had received thymic radiation. The other 11 children had received irradiation to the tonsils, adenoids, cervical lymphatics, or chest for various benign conditions. Berard and associates[9A] reported three instances of thyroid cancer after radiation at 4, 6, and 8 years of age for benign laryngeal papillomata. The long intervals of 22, 29, and 11 years, respectively, between x-ray therapy and the diagnosis of thyroid cancer suggest that longer follow-up studies on present series might yield additional cases. These cases are not included in table 1, since all were too old for this report when the diagnosis was established.

TABLE 2.—*Findings in Ten Children with Carcinoma of the Thyroid*

Case, No.	Sex	Age, Yr., and Date at Time of Diagnosis	Histology of Tumor	Age at Time of X-ray Therapy, Yr.	Area Treated	X-ray Dose, r	Interval Between X-ray Therapy and Cancer Diagnosis Yr.	Follow-up Period and Remarks
1................	M	11, 1957	Papillary	1	Thymus	600	10	Living with lung metastasis, 9 mo.
2................	F	10, 1954	Papillary	2	Tonsils and adenoids	Unknown	8	Living with lung metastasis, 4 yr.
3................	M	11, 1938	Papillary	6	Neck	5 x-ray treatments	5	Living with no evidence of disease, 14 yr.
4................	M	6, 1953	Papillary	5 mo.	Thymus	500	5½	Living with no evidence of disease, 4 yr.
5................	F	16, 1951	Adeno-carcinoma	7	Chest, neck	320	9	Living and well, 3 yr.
6................	M	17, 1956	Papillary	7 wk.	Thymus	800	17	Living with no evidence of disease, 1 yr.
7................	F	7, 1955	Adeno-carcinoma	6 mo.	Thymus	600	6½	Living with no evidence of disease, 1 yr.
8................	M	10, 1955	Follicular	No therapy	...	...	...	Living and well, 3 yr.
9*................	M	17, 1954	Hurthle cell	...	...	...	...	Living and well, 2 yr.
10*................	M	12, 1953	Undifferentiated carcinoma	...	...	...	...	Living and well, 5 yr.

* No definite positive or negative statement could be obtained regarding previous irradiation therapy.

Summary of Cases

Six cases of carcinoma of the thyroid in children have been observed at Emory University Hospital in the past 20 years. Four additional cases[10] were located in the records of other Atlanta hospitals. These 10 patients represent all the recorded cases of carcinoma of the thyroid which were diagnosed in children under the age of 17 in the six major Atlanta hospitals. Seven of these 10 received irradiation in early childhood for various benign conditions. The findings in these 10 patients are summarized in table 2.

We have found, as have other authors, that in most cases there is no positive or negative statement on these patients' records regarding previous radiation. In only one of our cases was a definite positive or negative statement recorded on otherwise extensive hospital records. This information must be obtained indirectly to avoid alarming the patient's parents. This indirect method, although quite time-consuming, enabled us to obtain a definite statement regarding previous x-ray therapy in 8 of 10 patients. In the other two patients no positive or negative statement could be obtained concerning previous radiotherapy, and, although we consider these patients as having received no previous irradiation, either or both of these could have had such treatment previously. If other authors encountered this same problem, it is quite possible that the percentage of children with thyroid neoplasm who received previous irradiation is higher than indicated in the literature. For example, no definite positive or negative statement was made regarding previous x-ray therapy in 12 recently reported cases[11] of thyroid carcinoma during childhood.

Data on technical factors is well presented by Simpson and Hempelmann.[7] All but two of their patients who later developed thyroid carcinoma were treated with ports measuring 6 by 8 cm. or larger. The two exceptions in which slightly smaller portals were used were newborn infants. Dosages ranged from 240 to 1,400 r on the skin, administered in one to five treatments. All of these patients had a tissue dose to the thyroid calculated at 180 r or more. Clark's[3] patients received from 200 to 725 r in air delivered through portals measuring from 3 by 3 to 10 by 15 cm. in one to six treatments. Our patients received from 320 r to 800 r in two to five treatments.

Summary and Conclusions

Ten cases of carcinoma of the thyroid in children 17 years of age or younger have been added to the recorded cases, bringing the total to at least 357. These 10 children represent all of the cases in this age group recorded in the six major hospitals of Atlanta, Ga. Seven of these 10 patients received previous x-ray therapy in infancy or in early childhood for benign conditions. These seven cases have been added to the reported thyroid cancers in children after irradiation, bringing the total to 121 cases.

Approximately one-third of all children with thyroid cancer received previous radiation therapy to the head, neck, or thorax. The diagnosis of carcinoma of the thyroid in children is increasing. This correlates, among other things, with the formerly prevalent use of x-ray therapy for benign conditions in early childhood. This correlation suggests that irradiation to the head, neck, or chest in infancy or in early childhood may be a causative factor in the development of thyroid cancer later in childhood. If it is valid, we should expect, in future years, a decrease in the incidence of this neoplasm in children as the practice of irradiating benign childhood conditions decreases or ceases.

Small quantities of radiation in infants or young children may be followed by thyroid cancer, but even large doses to the thyroid area in older persons are apparently not followed by an increased incidence of this neoplasm and its use in adults when indicated should not have to be restricted. Further studies are needed before definite conclusions can be reached. Until that time, young children should be protected from all ionizing radiation with few or no exceptions in the treatment of nonmalignant conditions.

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SERUM MAGNESIUM IN RENAL DISEASES.—Serum magnesium values have been determined on 40 healthy adults and 32 patients with various types and stages of renal disease. Serum magnesium in the normal group was 1.48 ± 0.17 mEq. per liter. Serum magnesium in the patients with renal disease was found to depend on the stage but not type of disease. The patients without azotemia occasionally had extremely low values, and one developed symptoms of magnesium deficiency. Azotemic patients, on the other hand, had elevated serum magnesium values. Patients with symptomatic uremia showed extremely high values. Serum magnesium correlated positively with blood nonprotein nitrogen and serum potassium. A significant negative correlation between total magnesium and calcium was observed, but the correlation became insignificant when the ionized portions of these cations were compared. Electrocardiograms revealed conduction defects in several patients with hypermagnesemia, but in only one case was this known to be the only electrolyte abnormality. Hypermagnesemia may contribute to the somnolence and eventual coma of uremia. Magnesium administration is contraindicated in marked azotemia.—W. O. Smith, M.D., and J. F. Hammersten, M.D., Serum Magnesium in Renal Diseases, *A. M. A. Archives of Internal Medicine*, July, 1958.

PROMETHAZINE HYDROCHLORIDE IN SURGERY AND OBSTETRICS

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Phenothiazine drugs have a potent sedative action, a marked antiemetic effect, and an apparent synergism with narcotics, barbiturates, and anesthetic agents. Preanesthetic medication with promethazine, scopolamine, and reduced doses of meperidine afforded optimal sedation without significant respiratory and circulatory depressions. Promethazine practically eliminated nausea and emesis in both the preoperative and operative periods, while the incidence of postoperative nausea and emesis after general anesthesia was reduced markedly. Induction and maintenance of general anesthesia was facilitated by promethazine, which appeared to reduce requirements of general anesthetic agents. Mild to moderate hypertension occurred in a few patients after the intravenous administration of promethazine; these rises in blood pressure were transient, without effect on the infant, and could not be explained. A number of patients presented bizarre athetoid-type movements and localized muscle twitchings after receiving promethazine; the muscular phenomena were easily controlled with small doses of intravenously given meperidine. In view of the proved epileptogenic properties of phenothiazine drugs, promethazine should not be given to patients with a history or evidence of preeclampsia, epilepsy, convulsions, intracranial trauma, and severe hypertension.

The phenothiazine derivatives possess pharmacological actions which are of considerable interest to the anesthesiologist. Phenothiazine drugs have a potent sedative action,[1] a marked antiemetic effect,[2] and an apparent synergism with narcotics, barbiturates, and anesthetic agents.[3]

Promethazine hydrochloride [10-(2-dimethylaminopropyl) phenothiazine hydrochloride] was studied by us in approximately 5,000 surgical and obstetric patients. This study was undertaken to evaluate promethazine as a premedicant drug, as an antiemetic agent, and as a sedative during spinal anesthesia.

Promethazine in Surgery

Promethazine was used in 4,300 surgical patients; the age distribution of these patients was 3 to 75 years. The operations performed included head and neck (225), tonsillectomy and adenoidectomy (567), plastic surgery (197), orthopedic (187), thoracic (85), cardiac and great vessel (55), peripheral vascular (450), abdominal (1,175), gynecologic (653), genitourinary (619), and rectal (87). Premedication was done in 2,800 cases with use of promethazine, meperidine hydrochloride, and scopolamine. In the 1,500 cases in which premedication was not done, promethazine was used as an adjuvant to spinal anesthesia.

The anesthetic method employed included local, spinal, and general anesthesia. The dosage schedules used in this study were as follows: For preanesthetic medication, the patient was given promethazine, 50 mg. intramuscularly at bedtime and 50-75 mg. intramuscularly 90 minutes preoperatively, meperidine, 50-75 mg. intramuscularly 60 minutes preoperatively, and scopolamine, 0.4 mg. intramuscularly 60 minutes preoperatively. For sedation and control of emesis during spinal anesthesia, the patient was given 25 mg. of promethazine intravenously. In pediatric cases, 0.5 mg. of promethazine per pound of body weight was given intramuscularly 90 minutes preoperatively and 0.5 mg. of meperidine per pound of body weight intramuscularly 45 minutes preoperatively, with appropriate doses of scopolamine.

Preanesthetic Medication.—Promethazine in combination with scopolamine and reduced doses of meperidine produced excellent sedation in the vast majority of patients (2,548 or 91%); the small group of unsatisfactory results (52 or 9%) occurred in early clinical trials with inadequate promethazine dosage. The characteristic preoperative picture was one of light sleep from which arousal was easy. Patient orientation and cooperation were excellent. The absence of respiratory and circulatory depression (hypotension) was noteworthy. We were impressed with the smooth induction of inhalation anesthesia; it was our definite opinion that drug requirements for maintenance of anesthesia were diminished. It was noted that the average patient's stay in the recovery room was somewhat prolonged; this slight delay in recovery, undoubtedly due to the promethazine, was characterized by a very light sleep, unaccompanied by circulatory

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and/or respiratory depression. We could elicit no unequivocal evidence that these patients were "protected" against stress or surgical trauma.

Sedation During Spinal Anesthesia.—Intravenously given promethazine (25 mg.) proved to be an excellent adjuvant for the sedation, without significant circulatory and/or respiratory depression, of patients under spinal anesthesia. Results were satisfactory in 1,455 cases (97%) and unsatisfactory in only 45 (3%). A single intravenous dose afforded dependable and predictable sedation for one and one-half to two hours. The peak of the sedative action appeared in 10 to 20 minutes after administration. The sedative effect varied from simple quiescence to light sleep from which arousal was easy. Pain or discomfort due to position or surgical manipulation were readily controlled with combined intravenously given doses of meperidine (10 mg.) and promethazine (10 mg.). Quite remarkable was the absence of hypotension and tachycardia; a solitary case of hypotension after the intravenous administration of promethazine occurred in an elderly patient with a history of autonomic imbalance.

Antiemetic Action.—Promethazine proved to be an excellent antiemetic. Its greater value appeared in the prophylaxis of narcotic-induced nausea and emesis, results were satisfactory in 98% of the cases, and in the active therapy of nausea and vomiting during spinal anesthesia, where results were satisfactory in 96%. A single dose of intravenously given promethazine (25 mg.) gave effective antiemetic action for one to two hours during and after spinal anesthesia. It was noteworthy that, where hypotension during spinal anesthesia was the cause of emesis, promethazine was no less valuable and did not aggravate the hypotension. Only slightly less effective was the antiemetic action of promethazine in the prophylaxis and treatment of postoperative nausea and vomiting (91% satisfactory results).

Side-effects.—A number of side-effects appeared in less than 1% of the surgical patients. These were moderate hypertension, localized muscle twitchings, and restlessness; all appeared after the intravenous administration of promethazine during spinal anesthesia. The latter two side-effects were readily controlled with small doses of intravenously given meperidine. The cause of the rare hypertension seen after promethazine was given is obscure.

Promethazine in Obstetrics

There has been a long search for a method of providing satisfactory obstetric analgesia and amnesia without maternal or fetal depression. To date, no ideal agent or combination of agents has been found.

Our experiences with promethazine in surgical patients suggested its application in the antepartum and intrapartum regimen. An unselected group of 700 obstetric patients received promethazine either alone or in combination with meperidine and scopolamine. Promethazine alone (25-50 mg. intramuscularly) was given to a group of patients in the antepartum period; no significant analgesia was observed. In 600 cases various combinations of promethazine, meperidine, and scopolamine were studied in the antepartum period. The optimal initial dosages appeared to be promethazine, 50 mg., meperidine, 75 mg., and scopolamine, 0.4 mg. (given intramuscularly or intravenously) or promethazine, 25-50 mg., meperidine, 100 mg., and scopolamine, 0.4 mg. Initial medication was given with the establishment of active labor or when the patient requested medication for pain relief.

The premedicant effect of these combinations was quite constant and predictable within 15 to 30 minutes after administration. The patients were well sedated and slept quietly. As intense contractions became forceful, they awakened quietly and returned to sleep with cessation of labor pains. They could be aroused easily and were cooperative. A single initial dose was necessary in 76% of the patients; the remaining 24% required supplementary sedation within two to four hours.

In the over-all group of 600 obstetric cases, premedication was considered satisfactory in 82% of the patients, as evidenced by a quiet, restful sleep and effective analgesia and amnesia. The incidence of nausea and emesis in all stages of labor was 3.6%. Hypotension and tachycardia were notably absent.

The promethazine regimen had no untoward effects on the infants, who showed good muscle tone and cried immediately on delivery or within 60 seconds thereafter. There were six stillbirths, all of which were known at the time of onset of labor. Three infants, subjected to prolonged and difficult delivery, required resuscitation; they responded rapidly to routine measures.

A control group of 330 unselected obstetric patients was studied. These patients were given premedication with secobarbital or pentobarbital (100-200 mg. rectally) and meperidine (100 mg.) with scopolamine (0.4 mg.) given intravenously or intramuscularly; supplementary doses of meperidine and scopolamine were administered as needed. Satisfactory analgesia and amnesia was achieved in only 60% of these patients. The incidence of nausea and vomiting was 27%. Fetal resuscitation was necessary in 25 (7.5%) as compared to only three cases in the promethazine group. This striking reduction in the incidence of fetal depression could not be related to any significant differences in meperidine dosages; it appeared to be related to the replacement of the barbiturates by promethazine in the antepartum regimen. In recently published studies,[4] we reported our failure to detect promethazine in fetal cord blood in spite of high maternal blood levels of promethazine. If promethazine does cross the placental barrier, it does so with difficulty and slowly, in contrast to the barbiturates.

Where general anesthesia was used for delivery, promethazine appeared to reduce significantly the anesthetic drug requirements. In the majority of cases, nitrous oxide was adequate, with or without pudendal block. Anesthetic induction and emergence were quiet and strikingly free of retching, nausea, and emesis.

In a group of 100 patients, not given premedication with promethazine, 25-50 mg. of promethazine was given intravenously to control nausea and emesis during spinal analgesia for cesarean section and vaginal delivery. All patients were relieved of nausea or emesis within three to five minutes. Hypotension and tachycardia were not observed. All infants cried immediately after delivery and showed no evidence of respiratory depression.

A variety of side-effects related to promethazine was seen. Mild to moderate hypertension occurred in a few patients after the intravenous administration of promethazine; these rises in blood pressure were transient, without effect on the infant, and could not be explained. A number of patients presented bizarre athetoid-type movements and localized muscle twitchings after receiving promethazine; the muscular phenomena were easily controlled with small doses of intravenously given meperidine. In three patients, generalized convulsions appeared in the antepartum period; one had a previous history of pre-eclampsia, while another was a known epileptic. The third patient had no history of earlier convulsions. The causal relationship of promethazine to these convulsions was uncertain. However, in view of the proved epileptogenic properties of phenothiazine drugs,[5] we now elect to avoid giving promethazine to patients with a history or evidence of preeclampsia, epilepsy, convulsions, intracranial trauma, and severe hypertension.

Summary

Promethazine, a phenothiazine derivative, was studied in 4,300 surgical and 700 obstetric patients. Clinical data and impressions were recorded on the effects and value of promethazine as an adjuvant in preanesthetic medication, as a sedative during regional anesthesia, and as an antiemetic agent.

In the surgical patients, the clinical data support the following conclusions: Preanesthetic medication with promethazine, scopolamine, and reduced doses of meperidine afforded optimal sedation without significant respiratory and circulatory depressions. Promethazine practically eliminated nausea and emesis in both the preoperative and operative periods, while the incidence of postoperative nausea and emesis after general anesthesia was reduced markedly. Induction and maintenance of general anesthesia was facilitated by promethazine, which appeared to reduce requirements of general anesthetic agents. Promethazine proved to be a valuable adjuvant in regional anesthesia for effective sedation without respiratory depression, tachycardia, or hypotension.

In the obstetric patients, the use of promethazine in the antepartum period effected excellent amnesia and analgesia, minimized nausea and emesis, produced no material depression (respiratory or circulatory), and decreased slightly the total narcotic requirements. The intrapartum and postpartum periods in these patients were characterized by a sharp decrease in nausea and vomiting during induction of and emergence from general anesthesia, smoother induction and lessened general anesthetic requirements, absence of maternal and fetal depression, and quieter emergence from general anesthesia.

Side-reactions to promethazine appeared rarely. These included restlessness, localized muscular twitchings, and moderate hypertension.

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The promethazine hydrochloride used in this study was supplied as Phenergan hydrochloride by the Wyeth Laboratories, Philadelphia.

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COMPARATIVE EFFECTS OF ANESTHETIC AGENTS ON CARDIAC IRRITABILITY DURING HYPOTHERMIA

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Factors affecting the incidence of ventricular fibrillation and asystole in hypothermia were studied in dogs. Four types of anesthesia were used and the responses of the heart to mechanical stimulation, hypercapnia, and hypoxia were observed. Temperature was found to be the most important factor, for fibrillation did not occur in 40 experiments at 27 C but was frequent in 50 experiments at 20 C. At the lower temperatures fibrillation was most often seen during cyclopropane-induced anesthesia and least often during anesthesia induced by thiopental-nitrous oxide supplemented with lidocaine. When the lidocaine was goven simultaneously with pentothal, subsequent induction of hypothermia to 20 C in 10 dogs resulted in spontaneous fibrillation in 4 and asystole in 1; in another series of 10 dogs, when lidocaine was given after hypothermia to 20 C had been induced, spontaneous fibrillation occurred in only 1, while asystole occurred in 4. No criteria were found that would distinguish hearts liable to fibrillation from hearts liable to asystole. Although the incidence of fibrillation was reduced with the use of lidocaine, there was an increase in heart block and asystole.

One of the serious disadvantages of hypothermia for surgical procedures is the development of ventricular fibrillation with degrees of hypothermia below 27 C (80.6 F). Investigators in this field have suggested that many factors are important in the onset of this arrhythmia.[1] Covino and co-workers[2] observed that the anesthetic agent used influenced the incidence of spontaneous ventricular fibrillation. Pentobarbital was found to result in a higher incidence of fibrillation than did thiopental or ether. Anlyan and associates[3] investigated the effect of mechanical stimulation, in the form of ventriculotomy, on the incidence of this arrhythmia. In this study, the frequency of ventricular fibrillation did not vary significantly with the three agents employed: ether, thiopental, and pentobarbital. Many adjunctive agents, including neostigmine (Prostigmin),[4] 2-(diethylamino-ethoxy) biphenyl (Dacorene),[5] and trimethaphan (Arfonad) camphorsulfonate,[6] have been used to suppress the onset of fibrillation during hypothermia with varying degrees of success. The establishment of an anesthetic technique which would prevent fibrillation in degrees of hypothermia below 27 C would extend the usefulness of this technique.

The successful use of lidocaine for defibrillation in both normothermic and hypothermic dogs[7] led to the study of the effect of this agent on the incidence of ventricular fibrillation induced by mechanical stimulation. Since cardiac massage is frequently required in these procedures, it was selected as the standard mechanical stimulus. The interrelationship of pH and pCO_2 with anesthetic management and the importance of these physiological variables in the onset of fibrillation during hypothermia[1] led to the inclusion of these factors in this investigation.

Methods

Mongrel dogs weighing between 5 and 14 kg. (11 and 31 lb.) were anesthetized with the selected agent, and endotracheal intubation was accomplished. Cyclopropane and diethyl ether anesthesia was maintained at a light level, as judged by the electroencephalogram. The amount of anesthetic agent was limited to that which would just prevent shivering and reaction to the endotracheal tube. Nitrous oxide was administered in a concentration of 50% with an equal part of oxygen. Thiopental was administered intravenously for induction in a dose of 20 mg. per kilogram of body weight and for maintenance in doses of 2.5 mg. per kilogram. Lidocaine was administered in one series in combination with thiopental (equal doses) and in others as a supplement in doses of 10 to 20 mg. per kilogram of body weight at 27 C after hypothermia had been induced. The femoral artery was cannulated and direct blood pressure tracings, together with electrocardiographic (lead 2) and electroencephalographic tracings, were monitored continuously during the experiment with use of a multichannel recorder. Hypothermia was produced by immersion of the dog in an ice-water bath until the body temperature had dropped to within 2 C of the desired temperature, 27, 23, or 20 C (80.6, 73.4, or 68 F). Temperatures were taken from either the rectum or esophagus with a telethermometer (Yellow Springs).

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A respirator and a to-and-fro absorption system were used throughout all experiments, and adequate ventilation was carefully maintained. After removal of the animal from the ice bath, the heart was exposed by means of thoracotomy and an incision of the pericardium. After stabilization at the desired temperature with the addition of 100% oxygen to the anesthetic atmosphere, arterial blood samples were taken and analyzed for oxygen, carbon dioxide, and pH. The heart was then subjected to a standardized pattern of mechanical stimulation consisting of 10 strokes with a blunt probe followed by two 30-second periods of vigorous cardiac massage at one-minute intervals. If failure or fibrillation ensued, resuscitation was instituted; otherwise, the dogs were ventilated for 30 minutes with addition of 10% carbon dioxide to the anesthetic atmosphere, the canister being removed. Blood samples were again drawn for analysis and the mechanical stimulation repeated. All surviving animals were ventilated for an additional 30-minute period with an anesthetic atmosphere containing 15% oxygen, the absorption canister again in place. At the end of this period blood samples were drawn and stimulus applied as before. Except for a small number of animals subjected to special studies, resuscitation was limited to the reestablishment of a regular beat and a blood pressure consistent with the temperature of the experiment.

TABLE 1.—*Results of Experiment at 27 C (80.6 F), Plus or Minus One Degree, with No Ventricular Fibrillation Occurring*

Agent	Dogs, No.	Control (100% Oxygen)			Hypercapnia (10% Carbon Dioxide)			Hypoxia (15% Oxygen)		
		pH	pCO_2	Oxygen, Vol. %	pH	pCO_2	Oxygen, Vol. %	pH	pCO_2	Oxygen, Vol. %
Cyclopropane	10	7.55	21.7	19.5	7.15	73.5	19.7	7.51	21.2	13.1
Diethyl ether	10	7.45	18.8	22.1	7.04	65.8	21.5	7.35	20.4	19.4
Thiopental and nitrous oxide	10	7.50	28.7	21.8	7.22	54.2	22.7	7.35	25.5	15.9
Thiopental, lidocaine, and nitrous oxide	10	7.57	21.7	23.2	7.19	70.5	24.1	7.55	32.2	19.4

Results

The onset of ventricular fibrillation did not occur in any of the experiments at 27 C, as shown in table 1. The blood values taken after the control period indicate adequate oxygenation and mild hyperventilation. The addition of 10% carbon dioxide is reflected in the low pH and high pCO_2 values. In a similar manner, the ventilation with 15% oxygen is reflected in the results of the blood analysis. After cardiac massage there were many periods of markedly abnormal electrocardiograms and periods of depressed cardiovascular function. Improvement in these conditions occurred with the removal of the stimuli and ventilation with oxygen.

The second series of experiments at 20 C resulted in the frequent occurrence of ventricular fibrillation, as indicated in table 2. In addition to the four anesthetization techniques used in the first study, lidocaine was given as a supplement after hypothermia had been established. The average temperature listed in the table is higher than 20 C, due to the onset of ventricular fibrillation before the lower temperature was reached. Differences between the anesthetic agents are indicated by the spontaneous incidence, as well as the over-all incidence, of ventricular fibrillation. The difference in the total fibrillations with cyclopropane as compared to the other agents is significant at the 5% level. Increased tendency for ventricular fibrillation with cyclopropane is also suggested by the high proportion of this arrhythmia, which was initiated spontaneously. Another difference noted in these results is the low incidence of fibrillation when lidocaine was used to supplement the thiopental and nitrous oxide. However, it is also apparent that there was a sizable increase in the number of dogs showing heart failure.

TABLE 2.—*Results of Experiment at 20 C (68 F), with Ventricular Fibrillation and Cardiac Failure*

Agent	Dogs, No.	Temperature, Degrees Centigrade	Ventricular Fibrillation		Failures, No.	Oxygen, Vol. %	pH	pCO_2
			Spontaneous	Mechanical				
Cyclopropane	10	23	8	2	0	22.0	7.55	17.0
Diethyl ether	10	21	4	2	0	16.0	7.49	12.4
Thiopental and nitrous oxide	10	21	3	2	0	19.0	7.64	19.7
Thiopental, lidocaine, and nitrous oxide	10	21	4	1	1	20.5	7.64	17.9
Lidocaine supplement to thiopental and nitrous oxide	10	20	1	0	4	18.3	7.68	14.9

Data for the final series of experiments, carried out at 23 C (plus or minus one degree), are listed in table 3. Ventricular fibrillation was prevented in all dogs except one. The hypercapnia and hypoxia portions of the study resulted in two additional failures in each series with a complex pattern of block and failure. The complexity of cardiac rhythm resulting from the combination of hypothermia, cardiac massage, and 10 mg. per kilogram of body weight of lidocaine as a supplement to thiopental–nitrous oxide anesthesia is illustrated in figure 1. In the second and third tracings of the electrocardiogram, the postmassage pattern at 23 C might be diagnosed as ventricular fibrillation if one did not have the simultaneous indication of a coordinated heartbeat in the lower tracing. Inspection and palpation of the heart also indicated that this was not fibrillation. In many instances levarterenol bitartrate was given to augment the cardiac contraction

TABLE 3.—*Influence of Lidocaine on Ventricular Fibrillation During Hypothermia at 22 to 23 C (71.6 to 73.4 F)*

Age Group	Dogs, No.	Ventricular Fibrillation	Failures, No.	Temperature, Degrees Centigrade	pH	pCO_2	Oxygen, Vol. %
Adults	10	1	1	22.7	7.5	15	22
Young	10	0	0*	22.6	7.4	25	19

* Varying degrees of heart block in four dogs reverted in one to three minutes with additional massage.

and blood pressure level. A different effect on cardiac conduction is revealed in figure 2. This tracing was taken on a pup who received 10 mg. per kilogram of body weight of lidocaine at 27 C during thiopental and nitrous oxide anesthesia. The 3:1 heart block which resulted in this experiment after massage disappeared during the next five minutes. Varying degrees and types of heart block were observed, including a number of examples of complete block, all of which reverted within a matter of minutes with supportive massage; levarterenol was given if cardiovascular depression was severe.

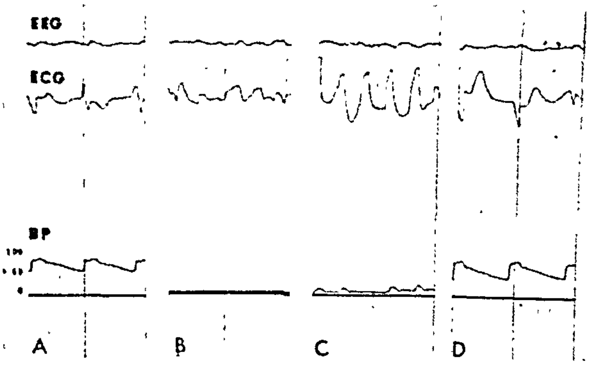

Fig. 1.—Electrocardiographic, electroencephalographic, and blood pressure tracings in dog with hypothermia at 23 C (73.4 F) after cardiac massage: *A*, control at 23 C; *B*, 45 seconds after massage; *C*, 50 seconds after massage; *D*, 65 seconds after massage.

Comment

The full advantage of hypothermia can only be realized if a means is found to control ventricular fibrillation and asystole. One of the factors influencing the onset of these arrhythmias is the choice of anesthetic agent. In this study, mechanical stimulation was added in the form of cardiac massage, since stimulation is an important factor in the onset of this process. It was also noted in preliminary studies that cardiac arrest in hypothermia frequently converted to fibrillation when massage was used in resuscitation. In the study at 27 C it was remarkable that no ventricular fibrillation occurred with any anesthetic agent despite the addition of periods of hypercapnia and hypoxia.

Discrepancy between these results and those reported previously[3] may be due to differences in experimental animals or type of stimulation. The employment of a greater degree of hypothermia, 20 C, indicates that there are differences in anesthetic agents in regard to the incidence of fibrillation. It is not apparent whether this finding with cyclopropane is related to its previously recognized properties as a factor in arrhythmias, namely, the production of ventricular fibrillation in the presence of epinephrine.

Lidocaine given as a supplement to thiopental-nitrous oxide anesthesia was effective in suppressing fibrillation, but the added depression resulted in a marked increase in the number of hearts which failed at this temperature. The dosage range of lidocaine which will prevent fibrillation and yet not produce arrest is very narrow.

No means were found which would indicate those hearts that might need protection from fibrillation or those that would be easily depressed. The problem of depression of the cardiovascular system led to the employment of slightly higher temperatures—22-23 C. As already noted, in two series of 10 dogs there was only one instance of fibrillation and one of failure. It is interesting to note that these both occurred in the adult series; however, the small number involved would not lend itself to drawing any conclusion. One of the problems encountered in this study was the diagnosis of ventricular fibrillation.

In the second tracing of figure 1 apparent fibrillation was the result of the cardiac massage. Within 15 seconds and with little change in the electrocardiogram, evidence of heartbeat appeared on the blood pressure tracing. Palpation and observation of these hearts revealed slow waves of contraction which increased in strength with time until effective heart beat could be demonstrated. It is likely that this represented some form of intraventricular block as the result of the hypothermia, massage, and drugs administered. A more recognizable pattern was also frequently seen, as illustrated in figure 2. Varying degrees of block up to complete heart block with ventricular asystole were observed in five of the young dogs for short periods of time. These usually reversed themselves with the passage of time, supportive massage, and small doses of levarterenol when the cardiovascular system seemed depressed.

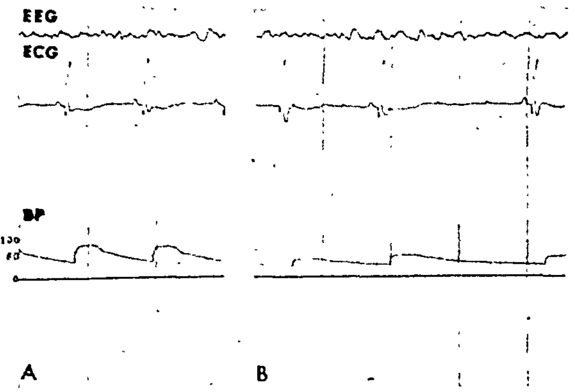

Fig. 2.—Heart block in dog with hypothermia at 23 C (73.4 F) receiving lidocaine after massage: *A*, 10:25, open thorax; *B*, after massage.

Lidocaine has been used successfully by Hitchcock and Keown[8] in suppressing arrhythmias during cardiovascular operations in both dogs and man. Although its depressant effect must be taken into consideration, it may prove useful in suppressing serious ventricular arrhythmias during hypothermia and extend the usefulness of this technique.

Summary

The effect of four anesthetic agents or combinations on the incidence of ventricular fibrillation in dogs during hypothermia was investigated. Arrhymias were initiated with the application of mechanical stimulation in the form of cardiac massage. At 27 C (80.6 F), there was no instance of fibrillation despite periods of hypercapnia and hypoxia. At lower temperatures cyclopropane anesthesia resulted in the highest proportion of this serious arrhythmia. Thiopental–nitrous oxide anesthesia supplemented with lidocaine markedly reduced the incidence of this arrhythmia; however, cardiac failure was a frequent occurrence. At a temperature of 22 to 23 C (71.6 to 73.4 F), failure was markedly reduced when lidocaine was used as a supplement.

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HOLISTIC APPROACH TO CLINICAL PROBLEMS OF HYPERSENSITIVITY

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The solution of clinical problems in allergy is dependent on (1) a recognition of the fact that an altered immunological response is present and (2) the employment of all possible means to avoid or modify the reaction. Consideration of six principles is necessary in the management of allergic patients: 1. Allergic persons are inherently capable of abnormal immunological reactions to normal environment factors. 2. They become sensitive to the agents exposed to in the greatest quantity and for the longest time. 3. Symptoms are usually the cumulative response to several sensitivities. 4. They usually involve the skin first, then eyes, nose, throat, trachea, bronchial tree, and alveoli, in that order. 5. Repeated attacks lower the critical sensitivity level of response so that subsequent exposures result in more severe symptoms. 6. Symptoms are modified by age, endocrine changes, climatic factors, and emotional stress.

In the treatment of hypersensitivity it is important to recognize that (1) many therapeutic efforts directed along single approaches have fallen short of the desired goal and (2) such approaches have produced results disappointing to the physician and the patient. With agreement that epinephrine (Adrenalin), aminophylline, antihistamines, antibiotics, and corticosteroids are useful and potent drugs and that psychotherapy is a useful modality, it remains that reliance on any one of these alone to solve problems in hypersensitivity leads to failure. This misplaced reliance confuses the physician's and patient's understanding of the problem.

In fact, the use of hyposensitization alone without proper identification, evaluation, and consideration of etiological factors, be they physical, chemical, immunological or psychic, is confusing, disappointing, and inadequate. All of these unfortunate adjectives apply too often in practice.

The solution of clinical problems in allergy is dependent on (1) a recognition of the fact that an altered immunological response is present and (2)

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the employment of all possible means to avoid or modify the reaction. The multiplicity of symptoms seen in many cases may confuse the physician and distract him from an awareness of the mechanisms involved. Often he resorts to futile symptomatic treatment without making an adequate attack on the etiology of the condition.

Six concepts which are fundamental to a sound program for the management of allergic conditions are listed below. The application of these concepts in each individual case will enable the physician to solve most of the problems of hypersensitivity which he encounters.

Development of Sensitivity

Immunological Reaction to Environment.—Allergic persons are those who are inherently capable of abnormal immunological reactions to normal environmental factors. The ability to develop immunity is essential to the preservation of biological integrity, but it is present to varying degrees in different persons. At one end of the scale are those anergic persons who show little or no immunological response, and at the opposite end are those overresponsive patients who show clinical symptoms of allergy. In the latter group the abnormal response may be (1) quantitative, with the formation of an unusual number of antibodies, and/or (2) qualitative, with the formation of abnormal antibodies capable of uniting with or being bound by the affected receptor cell. In the allergic person, tissues containing the cell-bound antibodies are the shock organs. In those who are nonallergic, neutralizing and/or blocking antibodies are stored largely in the serum and subcutaneous tissues.

Sensitization is possible even in relatively nonreactive persons if the exposure is sufficiently prolonged or the agent sufficiently antigenic, as, for example, poison ivy. It has been shown also that variations in reactivity occur in cells which have not been previously sensitized.

Amount of Exposure.—Allergic persons become sensitive to those agents to which they are exposed in the greatest quantity and for the longest period of time. Of the air-borne inhalants, house dust and, in the Ohio area, ragweed pollen and some fungi are prevalent in the greatest quantity and for the longest time; hence, these are the ones most likely to produce sensitivity. Frequently the patient's statement that he cannot be sensitive to citrus fruit (or some other food), because he eats it every day, will give a clue to the antigenic agents involved by pointing out the materials to which he has had the heaviest and most prolonged exposure.

Formation of Symptoms.—Symptoms are usually the cumulative response to several sensitivities. The degree of these individual sensitivities depends on (1) the antigenicity of the agent involved and (2) the amount of material to which the patient is exposed, as well as the duration of the exposure. Each of the sensitivities in operation at any given time, however, contributes to the patient's total degree of sensitivity, which determines his symptomatic response. Each allergic patient possesses a "critical level of sensitivity" at which he responds with symptoms. Only when his own "critical sensitivity level" is reached or exceeded will symptoms appear.

The antigenic materials contributing to each person's sensitivity are best identified by the history and only secondarily by such procedures as skin tests and elimination diets. Once the sensitizing materials have been identified, the patient should be instructed to avoid them, so far as possible. The education of the patient is the most valuable part of his treatment. It should not only acquaint him with the nature of his difficulties but also teach him the mechanisms for avoiding or minimizing his exposures. He should be taught to avoid not only those antigens to which he is already sensitized but also those to which exposure is likely to result in future sensitization. Hyposensitization is undertaken only when the total degree of exposure to all allergens cannot be held at a level well below the patient's critical sensitivity level. Only those antigenic agents which cannot be avoided are ordinarily included in the hyposensitization program.

Clinical Symptoms and Their Modification

Early Recognition of Allergy.—Clinical symptoms usually involve the skin first and then the eyes, nose, throat, trachea, bronchial tree, and alveoli, in that order. Gastrointestinal symptoms occur most frequently early and late in life and vascular symptoms in later life. The progression from one site to another may be slow or rapid, and in some patients clinical symptoms of allergy do not have their onset until late in life. Symptoms may occur in several sites, or shock organs, simultaneously. While it is true that some antigens tend to involve certain tissues more frequently than others, any antigen may produce symptoms in any tissue capable of responding as a shock organ. Ragweed pollen, for example, may produce eczema of the feet and legs.

This concept helps the physician to identify allergic patients early in life and, by anticipating further symptoms, to prevent more serious sequelae.

Effect of Repeated Attacks and Exposure.—Repeated attacks of clinical allergy lower the critical sensitivity level of response, so that subsequent exposures to antigens result in more severe symptoms. During the ragweed season, for example, symptoms increase in severity after two to four weeks, though the pollen count is receding at this time. Thus, it is important to avoid continued and prolonged exposure to any potential antigen. It is equally important to relieve symptoms by whatever means are available. Therapeutic measures include (1) antihistamines for blocking the action of histamine, (2) aminophylline and epinephrine to counteract the end-effects of smooth muscle spasm and increased capillary permeability, (3) sedatives to reduce stress, and (4) corticotropic hormone for rendering the shock organ more resistant to reaction or for inhibiting antibody response.

Modifying Factors.—Symptoms or sensitivity responses are modified by age, endocrine changes, climatic factors, and emotional stress. The infant may be sensitized in utero, but much more commonly sensitively develops only after constant reexposure over many years.

At times when major shifts in endocrine balance occur (at approximate ages of 1, 6, 12, 45, and 65 years and during or after pregnancy), the type, site, or manner of allergic response in a sensitive person is likely to undergo radical change. This fact has given rise to the erroneous concept that at those ages persons are likely to "outgrow" their allergies. As a result, the program of allergic management is often withdrawn, causing the patient's sensitivities to increase and symptoms to reappear with increased intensity and in new shock organs.

Climatic factors, which include humidity, temperature, and barometric pressure, may vary with the time of day, season, or geographical location. When the humidity is high, respiratory effort is increased and air-borne antigens are concentrated near the ground. A rise in temperature aids in dispersing these antigens. It has been found that pollen and fungus spores in the atmosphere, which are dispersed to a height of 12,000 to 15,000 ft. on a sunny afternoon, may be concentrated in the lower 800 to 1,000 ft. between 3 and 4 a. m.

The critical level of response to antigens may be raised temporarily by emotional stress, but when such stress is continued the critical sensitivity level is usually lowered. This pattern of response to stress is similar to that described in Selye's general adaptation theory.[1] Many patients have symptoms only when they are emotionally exhausted.

Knowledge concerning the factors modifying sensitivity responses may enable physicians to anticipate situations which may call for extra precaution. Any one of these modifying factors may be important enough at a given time to prevent or produce clinical symptoms.

Summary

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MANAGEMENT OF CHRONIC URTICARIA

Ben C. Eisenberg, M.D., Huntington Park, Calif.

Analysis of 50 cases of chronic urticaria revealed a large variety of foods, drugs, infections, inhalants, and other items as possible causes of the disorder. The patients ranged in age from 8 to 73 years, and some had been afflicted as long as 22 years. There was much overlapping of etiological diagnoses. Emotional difficulties appeared to be significant in 32 patients, but among these there were only 6 in whom no other factors were clearly operative. Patients were encouraged to discuss domestic and occupational situations that might be emotionally charged. When the cause eludes recognition or cannot be obviated, symptomatic treatment is necessary. In this series it usually consisted of hydroxyzine hydrochloride, given orally in doses of 10 to 25 mg. three or four times a day, with antihistamines. Ephedrine hydrochloride was occasionally given by mouth and seldom by injection. Injection of epinephrine may be required in an occasional patient in whom angioneurotic edema threatens life by involving the pharyngolaryngeal areas.

Despite the addition in recent years of ACTH and corticosteroids to the list of drugs effective in combating allergic diseases, chronic, recurrent urticaria continues to present a therapeutic challenge to the ablest of specialists. All are familiar with the lesions typifying the urticarial reaction, namely, the circumscribed, edematous, blanched wheals surrounded by erythematous flares and attended by varying degrees of itching, pain, or burning. About half of the cases are accompanied by localized or rather extensive angioneurotic edema, and some patients may even show marked dermographia. The onset of hives may be gradual or sudden, with disappearance of the rash in a few hours or days and reappearance at any time of the day or night, sometimes with greater intensity, in the same or different areas.

As to the incidence of urticaria, various investigators estimate it to be from about 15 to 24% of the population, with chronic urticaria occurring more commonly in the third and fourth decades, especially in women.[1]

It is important to rule out several other conditions in the differential diagnosis of urticaria, namely, insect bites (flea, mite, bedbug, gnat), viral disease, herpes, hypersensitivity to light, heat, or cold, elephantiasis nostras, urticaria pigmentosa, and collagen disease (i. e., polyangiitis and lupus erythematosus disseminatus). Occasionally, contact dermatitis and atopic eczema may show localized areas of whealing and angioneurotic edema, but complete history and physical examination usually lead one to the correct diagnosis.

Causes of urticaria may be generally classified as allergic, nonallergic, and psychogenic. Allergic agents include drugs (aspirin, sedatives, antibiotics, cathartics, tranquilizers, cold remedies, beverages, vitamins, antihistamines, ACTH, herbs, estrogenic and other hormones, insulin, anticonvulsants, serums, vaccines, nose drops, and douching powders), foods (fresh fruits, nuts, chocolate, seafoods, pork, eggs, milk, and wheat), physical agents (sunlight, heat, cold [cryoglobulinemia], air currents, pressure, and ultrasonics), inhalants (pollens, house dust, castor bean dust, cottonseed, flaxseed, cosmetics, aerosols, insect debris, pyrethrum, orris, derris, antibiotics, molds, animal dander, animal secretions, and cooking odors), contactants (ointments, lotions, cosmetics, animal secretions and dander, soaps, detergents, serums, antibiotics, chlorpromazine [Thorazine] hydrochloride, shampoos, plants, grasses, and weeds), and autoantibodies (to hormones, protein degradation products, by-products from infections, and haptenes).

Nonallergic causes include infection (genitourinary, gastrointestinal, respiratory, dental, tonsil, and gallbladder, malaria, intestinal parasites, brucellosis, and syphilis), endocrine imbalance (excess or deficiency), i. e., hypothyroidism, enzyme imbalance (excess or deficiency), histamine and serotonin liberators (sorbitol monolaurate compounds, polyvinyl pyrrolidone, serums, peptone, trypsin, bacterial toxins, curare, narcotics, egg-albumin, and dextran), and miscellaneous causes (malignancy, neoplasms, lymphomas, diabetes, collagen disease, alcohol, insect bites, chemical and exhaust fumes, paints, hair sprays, trauma, exertion, and hereditary angioneurotic edema).

Psychogenic causes are of three types: (1) pure or cholinergic (emotional factors as sole cause, hypnotic recall, patient trapped by some resentful life situation, exciting events, and production of hives at will to avoid unpleasant situations), (2) mixed (emotional factors only one of several etiologies but equal in importance to other factors), and (3) masked (urticarial lesions as a manifestation of impending mental breakdown).

From the Medical Department, University of Southern California School of Medicine, and the Allergy Clinic, Los Angeles County General Hospital.

Read in the Session on Allergy before the Section on Miscellaneous Topics at the 107th Annual Meeting of the American Medical Association, San Francisco, June 27, 1958.

Both the acute and chronic types of urticaria can be precipitated by similar causes. Although most acute attacks of hives last only a few days, some may not subside until a period of three or four weeks have passed. This is not infrequently seen after reactions to penicillin and other drugs. Chronic urticaria, which may persist for many weeks, months, or years, sometimes follows acute episodes. In these instances other causative agents, such as dormant allergies to foods or inhalants, psychogenic factors, or hypersensitivity to heat or cold, take over, so to speak, and continue to perpetuate the reaction long after the original inciting agent has been metabolized, excreted, or destroyed.

One who has had an opportunity to observe and study patients with chronic urticaria cannot help but feel that they are endowed with an innate capacity to produce urticarial lesions at the slightest provocation, once the reaction has been facilitated by any means. Thus, it is not at all unusual for many of these persons to develop hives, regardless of the main etiology, after upper respiratory infections, minor trauma, exposure to chemical fumes, administration of almost any drug (i. e., vitamins, hormones, sedatives, aspirin, vaccines, and antibiotics), even in the absence of true allergy to these substances, and in response to any nonspecific factor that may upset the equilibrium, routine, or comfort of the patient, such as headache, physical or mental fatigue, gastrointestinal upset, alcohol, emotional excitement or anger, or undue exposure to heat or cold. In short, many things which are harmless to the average person become "urticariogenic" as far as these individuals are concerned, causing the release of histamine or acetylcholine into the skin, with resultant itch and wheal development.

In the management of chronic urticaria, a comprehensive history is most essential. Practically all of these patients have consulted several physicians and have tried all sorts of therapies prior to their referral to an allergy specialist—a last resort. It is important, therefore, that ample time be scheduled for the taking of a detailed history, including a thorough medical survey. One should especially consider the four factors listed by Sheldon and co-workers [1a] as the most common causes of hives and angioneurotic edema, namely, drug allergy, food allergy, infection, and psychic factors, and rule them out one by one. Also, it is imperative to inform these patients that intensive studies are often required before a proper etiological diagnosis can be made, that they must not expect too much until the causes are known, but that, in the meantime, effective drugs will be given to afford some, if not complete, relief of the pruritus and swelling.

Investigation of Specific Allergies

Drugs.—As was pointed out by Brown,[2] reactions to drugs have increased remarkably in recent years, particularly since penicillin and other antibiotics have been introduced. Patients must be questioned carefully concerning penicillin injections, recent and past, since urticaria may not begin until two or more weeks after its administration and may persist for months afterward. Also, one should inquire about other injectable or oral medications, such as vitamins, estrogen and other hormones, ACTH, antibiotics, insulin, cathartics, aspirin, tranquilizers, sedatives, tonics, alcoholic beverages, digitalis, mercurial diuretics, iodides, thyroid, procainamide (Pronestyl) hydrochloride, quinine, sulfonamides, nose drops, eye drops, suppositories, ointments, contraceptives, biologicals, aminosalicylic acid, hydantoins, heparin, and phenylbutazone.

In attempting to evaluate drug allergy, it is best to have the patient stop all medication—both oral and parenteral—and then observe whether the skin lesions disappear. Attempts may be made to reproduce the urticaria by giving small doses of the suspected drug, but this must be regarded as a dangerous procedure. Fatal anaphylactic shock has been reported after ingestion of a single penicillin tablet by a patient sensitive to this drug. One of my aspirin-sensitive patients suffered an anaphylactic reaction with severe asthma and loss of consciousness for several hours after ingestion of a tablet containing 2½ grains (160 mg.) of aspirin in combination with an antihistamine for a "cold." He made an uneventful recovery after energetic treatment with epinephrine, oxygen, and intravenous administration of aminophylline and hydrocortisone.

Food.—As most physicians know, patients generally are able sooner or later to identify the foods causing their urticarial outbreaks. Nuts, shellfish, berries and other fresh fruits, eggs, chocolate, and pork are common offenders. The diagnosis becomes more difficult when the case is a chronic one due to foods eaten daily, such as cereals, milk, vegetables, and meats. Furthermore, these substances tend to produce delayed reactions after an interval of 24 or even 36 hours. Nevertheless, the patient's food habits, his likes and dislikes, and regularly eaten foods should be listed and discussed, with a view toward eliminating any one or more from the diet for a trial period. The relationship between food allergy and urticaria is further complicated by the fact that the clinical sensitivity may be due to food additives or to antibiotics given to animals prior to human consumption. Milk, for example, may contain not only penicillin (if such is given to the cow for treatment of infection) but also antigenic amounts of alfalfa and beet-top proteins where these are grown and used as cattle feed.

At the allergy clinic of the Los Angeles County General Hospital, we feel that skin testing for food allergy is helpful in a sufficient number of patients to warrant its continued use. This is especially so if one employs for testing purposes the acetone-precipitated food-protein antigens dissolved in a phosphate-buffered 50% solution of glycerol.[3]

Infection.—Investigation of chronic urticaria cases should include possible sources of infection as primary causes of the eruption. Intestinal parasites must be ruled out in patients with a relatively high eosinophil count. Cohen and Criep[4] found amebic infestation to be the cause of recurrent urticaria with angioneurotic edema in 19 of 28 veterans. Hookworm and Giardia lamblia have also been recovered from the stools of patients with urticaria.[5] Eradication of these parasites resulted in ultimate cures. Other sources of infection related to outbreak of hives include tonsils, teeth, gallbladder, and genitourinary tract.

The exact mechanism by which infection precipitates urticaria is not known. If one is permitted to postulate, however, it is certainly not outside the realm of possibility that infectious processes, through breakdown of body tissues, bring about the release of active protein-splitting enzymes capable of mediating the urticarial response secondarily through liberation of serotonin, histamine, or acetylcholine into the skin. In addition, this same result may be accomplished by the production of autoantibodies and their subsequent reaction which the specific inciting haptene. Eradication of infection through surgical means or the judicious use of antibiotics, antimalarial agents, or antiamebic drugs should largely help to eliminate infection as a prominent cause of chronic urticaria.

Inhalants and Miscellaneous Agents.—Pollens, molds, house dust, castor bean dust, and animal danders have been found to cause outbreak of hives in numerous individuals. Insect sprays, hair sprays, perfumes, odors of cooked or fried foods, and various chemical fumes may likewise cause urticaria and angioneurotic edema. Cases of hives have developed during the course of various diseases, such as diabetes, endocrine disturbances, carcinoma, undulant fever, rheumatic fever, and syphilis. And, finally, contactants, i. e., animal danders and secretions, cosmetics, drugs (streptomycin, chlorpromazine), animal serums, weeds, and plants, have been occasionally responsible for this dermatological condition.

Psychogenic Factors.—Considerable disagreement still persists regarding the incidence of psychogenic factors in chronic urticaria. Because the immunological approach often fails to reveal a causal relationship between a drug, food, or other allergic factor and chronic urticaria, various investigators feel that most of these patients develop hives on an emotional basis.[6] It has been known for some time that emotional reactions can result in the liberation of histamine and acetylcholine into the skin to initiate the urticarial reaction. Hence, many physicians conclude that chronic urticaria is usually produced psychogenically.[7]

Just because extrinsic factors cannot be implicated after a brief visit with the patient is no reason to jump to the conclusion that the condition is caused *solely* by emotional factors. This diagnosis should not be made without a thorough allergic and psychological evaluation. Emotional disturbances are common today, just as they have always been, and may have little bearing on the patient's dermatological condition. Some individuals who are keenly aware of the impact of the psyche on disease processes may interpret a sign or symptom too readily as of psychogenic origin. In this manner, the initial pruritus of Hodgkin's and other organic diseases has often been mislabeled as due to emotional causes. We must not forget, however, that itching may arise from profound emotional disturbances. True, the discomfort attending urticaria and angioneurotic edema may cause the patient much distress of mind, but it is within the physician's realm to determine whether the distress is excessive for the condition at hand. Hives have often been reproduced in hypnotized subjects by psychotherapists during discussion of emotionally charged material; furthermore, cases of chronic dermatitis (eczema, neurodermatitis) have been treated successfully by means of psychotherapy and electroshock therapy.

Although no studies thus far have tended to prove a definite personality type in psychogenic urticaria, most observers agree that these patients have certain emotional conflicts in common: (1) chronic frustration, often originating in early childhood; (2) feeling of being "trapped" by some resentful situation about which they cannot, or dare not, do anything; (3) repressed aggressiveness, fury, and hostility; and (4) feelings of guilt because of fancied retaliatory measures and ill-wishes directed toward those responsible for their predicament.

"Total" Approach to the Urticaria Problem

The main purpose in presenting this paper is to show what may be accomplished by a "total" plan of treatment for chronic urticaria. This approach includes a comprehensive history and physical examination, sufficient laboratory work to exclude infectious processes, skin tests for allergy to foods, inhalants, pollens, and environmental factors, and a reasonable psychological evaluation of the patient. In my opinion, recurrent urticaria, with the exception of that caused by infection or drugs, is seldom due to just a single factor but rather to multiple causes, some of which cannot be determined by presently known methods of testing.

Fifty patients suffering from chronic hives were studied with use of this plan of attack. As noted in the table, their ages ranged from 8 to 73 years, with most in the 20-to-60-year age group, and females predominated (31 females, or 62%). Duration of the urticarial symptoms ranged from one month to 22 years.

While a single agent was responsible for some of these patients' symptoms, the majority revealed multiple etiological factors. Thus, foods were implicated in 24 patients or 48%, drugs in 11 (22%), infection in 6 (12%), emotional factors in 32 (64%), and inhalants in 22 (44%). Eighteen (36%) of the group suffered from hay fever, asthma, or allergic headache. This undoubtedly accounts, in large measure, for the higher percentage of positive findings in skin tests as compared with other series of chronic urticaria cases.

Data on Fifty Cases of Chronic Urticaria

Case, No.	Sex	Age, Yr.	Duration of Disease, Yr.	Allergy Findings					Results		Additional Diagnosis
				Foods	Drugs	Infection	Emotional Cause	Inhalants	Improved	Unimproved	
1	F	73	1	Fish, pork, egg-white	Estrogen		+	Wool, jute	+		
2	F	59	2½	...	Phenobarbital			...	+		
3	M	28	10	...	Penicillin			Pollens, house dust	+		
4	F	56	10	Negative findings			+	Negative findings	+		
5	F	15	½	Chocolate, egg-white			+	Feathers, cat	+		Hay fever
6	F	65	7	Chocolate, pork, coffee			+	...	+		Asthma
7	F	49	½	...	Reducers			Cotton, pyret	+		Hay fever
8	M	32	¼	...				Pollens		+	
9	M	57	½	No tests	Antibiotics	+		No tests		+	*Ulcerative colitis*
10	M	32	¼	...				Feathers, house dust	+		Headache
11	F	17	1	Milk, egg-white			+	House dust, kapok	+		Asthma
12	F	50	3	...			+	...	+		Hay fever
13	M	53	5	Legume, fruits			+	...	+		
14	M	31	1/12	Pork, chocolate	Toxin-antitoxin tests			House dust, pollen	+		Hay fever
15	F	21	2	Wheat			+	Orris, house dust	+		Hay fever
16	F	37	12	Pork, citrus, milk			+	...	+		
17	F	66	10	No tests			+	No tests	+		
18	F	54	1	Negative findings			+	...		+	
19	M	14	2	Wheat, egg-white, chocolate	Influenza vaccine			Feathers, pollen	+		Asthma
20	M	37	1½	...			+	House dust		+	Hay fever
21	F	20	½	Negative findings			+	...	+		
22	F	28	8	Negative findings			+	...		+	
23	F	24	2½	Wheat, milk			+	...			
24	M	34	¾	No tests	Antibiotics	+		No tests	+		Arteritis
25	F	19	6	Fruits		+	+	House dust	+		Recurrent herpes
26	M	34	1/12	...			+	...		+	Schizophrenia
27	M	33	1	Fish		Sinus		House dust	+		Asthma
28	F	48	1/12	No tests	Phenobarbital, penicillin			No tests	+		
29	M	8	4	Milk			+	...	+		Hay fever
30	F	28	17	...			+	Cat, feathers	+		Postpoliomyelitis
31	F	44	3	No tests	Antibiotics			No tests	+		Hyperthyroid
32	M	25	13	Pork, wheat, milk			+	Pollen	+		Asthma
33	M	48	3	Egg-white, chocolate	Vitamins	+		Pollen, house dust	+		Prostatitis
34	F	14	1/12	Fruits, fish			+	...	+		Asthma
35	F	32	13	...			+	Pollen, house dust		+	Asthma
36	M	36	1/12	Pork			+	...		+	
37	F	50	2	Fish, egg-white			+	Pollen, house dust	+		Asthma
38	F	25	¼	Shrimp, wheat			+	...		+	
39	F	35	½	...			+	...	+		
40	M	72	22	Fruits, wheat, milk				...		+	
41	M	32	½	Cereals				...	+		
42	F	38	10	...			+	...		+	
43	F	43	3	...			+	Pollens	+		Hay fever
44	F	53	3	...			+	Mold, wool	+		
45	F	19	¼	No tests			+	No tests		+	
46	M	35	3	No tests				No tests	+		Chemical fumes
47	F	37	16					Cat, dog, pollen	+		Asthma
48	F	52	14	Nuts, cereals		+		Pollen, house dust	+		Bronchitis
49	F	55	1	Chocolate			+	...		+	
50	M	24	½	Wheat, citrus			+	...	+		

Treatment.—Patients were advised to avoid all foods for which they showed 3+ and 4+ skin test reactions for approximately one month, and were started on a hyposensitization program with use of extracts of the inhalants to which there were positive reactions. Also, all previous medication was stopped, including cathartics, sedatives, estrogen, antibiotics, food supplements, and vitamins. Length of treatment varied from two weeks to two and one-half years, averaging approximately eight months per patient. Most of those continuing on allergy care past a six-month or eight-month period were advised to do so because of additional allergic conditions (i. e., asthma, hay fever, or allergic headache). Meanwhile, those evidencing probable underlying emotional difficulties, as revealed from observation and general discussion concerning job, home, and school situations during the preliminary examination and testing period, were singled out for special attention along these lines. Thirty-six patients, or 72%, improved under this regimen.

Symptomatic Care.—Most of the patients were able to control the hives and itching with antihistamines alone or in combination with ephedrine hydrochloride and tranquilizers. I seldom administer epinephrine or ephedrine by injection, since this mode of therapy almost invariably tends to temporarily "dam-up" the chemical forces responsible for the eruption, only to have the process recur with greater intensity after the sudden release of these chemicals when the action of the above-mentioned drugs subsides. Of course, epinephrine may be required in an occasional patient in whom angioneurotic edema threatens life through involvement of the pharyngolaryngeal areas. Here, ACTH and the corticosteroids may be found necessary. These latter two, however, are seldom of much benefit in chronic urticaria and should not be used because of dangerous implications after their long-term use (such as osteoporosis or enhancing infections).[8]

Tranquilizers.—While most tranquilizers may be tried for their ataractic effect,[9] I have found hydroxyzine (Atarax) hydrochloride[10] to be more effective in chronic urticaria. This drug is given in a dosage of 10 to 25 mg. four times a day. The relief of itching and hives is often dramatic.

Ephedrine and antihistamines, given orally, may be used in addition to enhance the beneficial result. The chemical formula of hydroxyzine is 1-(*p*-chlorobenzhydryl)-4-[2-(2-hydroxyethoxy)ethyl]piperazine dihydrochloride. It has been shown to exert antihistamine, antiserotonin, and anticholinergic effects and will neutralize the actions of such spasmogenic agents as barium chloride, posterior pituitary, and reserpine. Pharmacological and clinical studies demonstrate the ability of this substance to produce ataraxia without undue drowsiness or significant effect on mental acuity; other effects include transient hypotension, increase of coronary blood flow, and reduction of the incidence and duration of epinephrine-induced ventricular arrhythmia.

For acute urticaria, or severe flare-ups in the chronic type, I have had success with one of the following combinations given intramuscularly: (1) 0.4 cc. of diphemanil (Prantal) methylsulfate (25 mg. per cubic centimeter) and 0.5 cc. of hydroxyzine (in the same concentration) or (2) 0.4 cc. of diphemanil methylsulfate and 0.5 cc. of promazine (Sparine) hydrochloride, both in the same concentrations as above. Epinephrine (0.3 cc. of the 1:1,000 solution) may be added to these mixtures, if indicated, as in life-threatening edema of pharynx and larynx. These same combinations may be employed for the relief of asthmatic attacks. The additional anticholinergic and ataractic effects provided by these medicaments apparently enhance the therapeutic effect of epinephrine in allergic conditions.

Comment

As yet, there is no fool-proof laboratory method for the diagnosis of food allergy. Despite the fact that skin tests for food allergies are not as reliable as those for pollen and environmental allergens,[11] the procedure is of aid often enough to warrant their use, provided good, active extracts are employed. Even extensive diet trials, elimination diets, and well-kept food diaries which include tabulation of time and intensity of symptoms often prove fruitless. Until a reliable serologic laboratory test is devised for the diagnosis of food allergy it must be realized that much so-called food allergy is iatrogenically induced. Try to convince a patient he is not allergic to certain foods once he has been handed a list showing which to avoid even on a trial basis! Nearly every physician has encountered patients who recite no end of foods to which they are supposedly allergic solely on the basis of previously prescribed elimination diets. Unless repeated trials or procedures, such as the "double-blind" technique, reveal definite results, patients should be informed of only the possibility of their being allergic to the foods showing positive reactions to tests, or which they are asked to delete temporarily from the diet. After a brief period of avoidance—about two to four weeks—these foods should be gradually added back to the diet, one by one. Certain foods, however, such as fish, nuts, eggs, or pork, may never be tolerated without allergic difficulty. In such instances the patient may have to avoid some foods for life.

Patients with chronic urticaria are unique, psychiatrically speaking, in that the majority suffer from some intolerable life situation which is responsible for much, if not all, of their symptoms.[12] The physical manifestations represent a "boiling-over" of forces generated by deep, unresolved emotional conflicts. Once the patient is helped to pinpoint and discuss the home, job, or other problem which vexes him, this pressurized "head of steam" quickly dissipates, often with dramatic improvement, if not complete subsidence, of symptoms. This sequence of events has been observed by many investigators.[13] Needless to say, those patients who deny the existence of emotional factors, which are nevertheless strongly suspect, should be referred to a competent psychiatrist for further help. Quite often, however, the patient will readily volunteer such information during the very first visit to his physician, provided (1) an understanding and unhurried approach is used and (2) the doctor takes the time to "hear the patient out."

The various complaint categories with respect to emotional difficulties encountered by this group of patients may be categorized as follows: First are family situations, including (1) irresponsible, abusive, alcoholic, or domineering husband and wife; (2) delinquent offspring or physically or mentally handicapped children; (3) separation of parents, divorce, serious arguments, or step-parents; (4) interference by relatives and in-laws; (5) jealousy or sibling rivalry; and (6) settlements of estates and inheritances or bickering by survivors.

Second are occupational factors, including (1) undue pressure on the job, long hours, or adverse conditions; (2) unreasonable boss or foreman; (3)

undesirable fellow-workers; (4) unhappiness caused by type of work; and (5) undue discrimination, i. e., promotion, recognition, or pay.

Third, social factors may include (1) disappointment in love, (2) difficulties with school, friends, or neighbors, and (3) legal entanglements, court trials, or arrests.

While some of the specific psychogenic factors responsible for production of urticaria in this group represent an immature emotional reaction to commonly encountered life situations, others could be classed as quite unbearable even by the most mature observer. What amazes one is the length of time certain individuals will tolerate a given situation before doing something about it. I have in mind a 66-year-old woman who suffered severe urticaria and angioneurotic edema for eight years before finally admitting that her life had been in constant danger during all this time from a psychotic husband.

Another patient, a man, noted his first attack of hives immediately after learning that his second offspring was found to be deaf and mute. It is not enough to give such persons a prescription or ACTH or to tell them they will have to learn to live with their problems; they must be permitted to unburden themselves, encouraged to share their troubles with others, and directed to the proper channel or agency for help and guidance. It behooves all physicians, therefore, to become acquainted with the various health and welfare departments and family counseling services available in their respective communities and to take advantage of their facilities.

In many instances the situations "aired" by the patients are impossible of solution; even so, improvement may result from their being "ventilated" and brought out into the open. No one knows the exact mechanism by which such relief is obtained, but, in all probability, the individual is helped by a hopeful, understanding, and encouraging physician to make a better adjustment to life's difficulties and to channel his energies more constructively, perhaps through some process of sublimation.

"Total" treatment of these patients—elimination from the diet of foods that may be suspicious and show positive reactions for a trial period, specific allergy management directed against significant inhalants and environmentals, and encouragement toward pinpointing and "giving vent" to the particular emotionally charged situation triggering the liberation of histamine or acetylcholine into the skin—will yield a successful outcome in the majority of persons who suffer from chronic urticaria.

Most patients who do not respond to this regimen have in all probability deep-seated emotional conflicts which often cannot be resolved even after intensive psychotherapy. Here, the physician must use "supportive" and symptomatic therapy. Some persons, for psychological reasons, need the skin response as an outlet for their emotional pressures which otherwise might result in serious mental breakdown. It is unwise, therefore, to try to force these patients into psychotherapy against their will. They must be gradually prepared for such an eventuality when it is felt such treatment may be the answer to the problem. It is amazing how many patients are helped, however, by being allowed to talk freely about their problems. On leaving, some will remark: "Thank you, doctor, I feel better already." And all the physician has done, perhaps, is lend a sympathetic ear and ask one or two indirect questions. How well this proves the old maxim: in order to heal the ills of the flesh you must also relieve the mind and emancipate the spirit.

Granted, at least one-fourth of patients with chronic urticaria will not improve even though every presently known therapeutic modality is exhausted. Treatment of these unresponsive persons must await the development of further knowledge concerning enzyme chemistry, synaptic physiology, autoimmunity, and hitherto undiscovered hormones of the endocrines and central nervous system. In the meantime, let us welcome these patients, counsel them, and treat them. Thus far, the best ingredient available for the treatment of chronic urticaria is the physician himself.

Summary

Chronic urticaria still presents a therapeutic challenge to the allergy specialist, despite the notable additions in recent years of the corticosteroids and other so-called wonder drugs to his armamentarium.

Fifty patients with persistent urticaria were studied and treated, with use of a comprehensive approach: (1) complete history and physical examination to rule out infection and parasitic infestation, (2) allergic investigation, including skin tests for foods and inhalant allergy, (3) investigation for drug allergy, and (4) psychological evaluation for possible emotional factors as the sole or contributing cause of the dermatological condition.

Considerable diagnostic overlapping was uncovered, with many individuals revealing multiple etiological factors. Thus, foods appeared to be significant in 48%, drugs in 22%, infection in 12%, inhalants in 44%, and emotional difficulties in 64% of the patients. Suspected foods, as revealed by dietary history and skin tests, were eliminated from the diet for a brief period, and specific immunological treatment instituted against the inhalants to which positive reactions were given. Thirty-six (72%), improved under this regimen. Eighteen (36%) showed evidence of other allergic conditions, such as hay fever, asthma, and allergic headache.

Patients were encouraged to pinpoint and discuss freely any emotionally charged situation suspected of perpetuating the symptoms. Successful outcome depends a great deal on the physician's attitude and approach to the problem. If he appears hopeful and encouraging and is willing to "lend a sympathetic ear," most of these patients will improve.

Symptomatic treatment, for the most part, consisted of oral administration of hydroxyzine (Atarax) hydrochloride, 10 to 25 mg. three or four times daily, in combination with antihistamines and, on occasion, ephedrine hydrochloride.

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THERAPY OF ACUTE ATTACKS OF ASTHMA IN INFANTS AND CHILDREN

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Many conditioning factors modify most disease processes, and those factors inherent in the age of a patient are among the most significant. Of all the diseases in which age factors exert an influence on the pattern, course, and, therefore, therapy of a disease process, one is hard-pressed to think of one in which the impact of age is greater than in acute and/or chronic asthma.[1]

This being true, the following comments on principles and specific therapeutic measures of necessity must be considered in the light of the influence of age on this symptom-complex, asthma.

Factors due to age that are of prime significance in influencing the therapeutic approach to the treatment of asthma in infants and children are as follows: 1. More labile homeostatic mechanisms frequently fail to adequately protect against rapid dehydration, acidosis, and vascular collapse.[2] 2. Proportionately smaller nasal and bronchial airways are more easily "blocked" by a given amount of edema or spasm.[1] 3. At certain ages of the child proportionately greater panic and/or fear of suffocation may occur when severe dyspnea and cough are present in an asthmatic attack. 4. Difficulty in achieving proper medication and fluid intake may occur due to lack of cooperation in the excited, panicked, and/or resistant child. 5. Greater variability in response and idiosyncrasy to certain antiasthmatic medications may occur (i. e., the paradoxical response to barbiturates or an idiosyncrasy to aminophyllin). 6. The child's own emotional struggle with his disease and its attendant anxiety is multiplied by the anxiety and frequently reflected

For specific treatment of acute attacks of asthma in children, certain basic procedures stand out as of prime importance: 1. Institute therapy early in an attack. 2. Perform bronchodilation. 3. Use sedation (this includes the parents, when indicated). 4. Maintain adequate fluid intake. 5. Combat infection vigorously if it exists. 6. Eliminate immediate sources of potent allergic substances. It is possible if the parents have been thoroughly instructed, to institute therapy very early in an attack—in fact, almost before it begins. When antimicrobial therapy is carried out in the allergic child it should be maintained to conclusion (including at least two afrebile days).

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overconcern of the parents. 7. Associated infections are frequent.[3] 8. Nutritional problems are superimposed.[4] 9. There exists a greater potential hazard in the use of steroids (i. e., the occurrence of varicella while the patient is on steroid therapy or the more frequent accident rate in children).

In the light of these considerations, certain definite principles may be outlined for the plan of management of acute asthma in infants and children. Needless to say, if a child is having uncontrolled polycyclic attacks of asthma, he should be evaluated by a competent allergist and, on the basis of careful allergic history and accurate testing, have all of the avoidance measures carried out as well as hyposensitization to unavoidable sensitizing airborne allergens.

For specific treatment of acute attacks of asthma in children, however, certain basic procedures stand out as of prime importance: 1. Institute therapy early in an attack. 2. Perform bronchodilation. 3. Use sedation (this includes the parents when indicated). 4. Maintain adequate fluid intake—hydration. 5. Combat infection vigorously if it exists. 6. Eliminate immediate sources of potent allergic substances.

For the purpose of this discussion, one may arbitrarily divide the treatment of acute attacks of asthma into (1) early mild to moderate attack and (2) more prolonged, severe attack (status asthmaticus). Actually, of course the latter is merely an extension of the former.

Acute Attack

Mothers of asthmatic children, as indeed older children themselves, can sense an impending attack of asthma. This is almost analogous to the aura of an impending epileptic seizure. In fact, some children have subjective feelings that are quite comparable to an aura. In addition to these subjective insights, a mother soon learns of certain objective factors that tend to precipitate asthma in her child, such as sudden changes in climate or temperature, periods of marked overexertion, "colds," certain emotional stimuli, and others.

It is possible, therefore, if the parents have been thoroughly instructed, to institute therapy very early in an attack—in fact, almost before it begins. This is when an attack of asthma is easiest to "block," for asthma tends to become progressive and fixed once it fully gets started.

Thus, at the first sign or prodrome of asthma the parents are instructed to give the child mild and properly balanced medication to effect bronchodilation and sedation. This mixture contains ephedrine and secobarbital in a palatable suspension (Aladrine). The proportion of ephedrine is sufficient for bronchial dilatation, yet it is "covered" by sufficient short-acting barbiturate to "block" the exciting effect of the ephedrine and also be sufficient for sedation of the child. For this, we have found the best proportion to be ⅛ grain (7.5 mg.) of ephedrine to ¼ grain (15 mg.) of secobarbital per teaspoonful. Further, as in epilepsy, wherein the proper amount of phenobarbital or other anticonsulsive agent is titrated to the demand of the individual child, also with this mixture the mother can learn just about how much is needed early to abort an asthmatic attack. In addition, secobarbital being a short-acting barbiturate, the medication may be repeated at four-hour intervals without fear of cumulative noxious effects as, for example, could be the case with long-acting phenobarbital. Thus, this mixture is simple and safe, may be "titrated," and meets the basic early needs. If one encounters a sudden severe acute attack, then, of course, aqueous epinephrine, 1:1,000, should be given immediately in appropriate doses (0.1–0.4 cc.). This then would be followed by the preceding regimen.

While bronchodilation and sedation is done in the child with asthma, the physician must also think in terms of keeping the secreted tracheobronchial mucus loose and liquefied should an attack progress. The best "expectorant" of all is fluid given by mouth, for the greatest cause of inspissation of mucus is dehydration of the little patient. When dehydration occurs and the extracellular fluid compartment is depleted, no amount of so-called expectorant will effect loosening and liquefaction of the mucus. Generally, dehydration is more frequently associated with more disease processes in the infant and child than in the adult. This is due to increased extrasensory fluid losses from a greater proportion of body surface to weight, frequency of associated diarrheal conditions and vomiting, and frequent lack of cooperation or understanding of the necessity of taking fluids, becoming more pronounced as the child becomes sicker and more dehydrated. Thus, the old, hackneyed phrase "an ounce of prevention is worth a pound of cure" has real application in fluid and electrolyte management of asthmatic infants and children,[2] for before the child becomes desperately ill, dehydrated, and gasping for air (for which he is more hungry than for food or fluid) one is able to get fluid into him. If there is associated vomiting along with the dyspnea, small amounts of fluid, neither too hot nor too cold, offered at frequent intervals may be more easily retained; this also gives the distressed parents a constructive job to do.

This, then, is the essence of the treatment of the early acute attack—bronchodilation, sedation, and hydration—early!

It ought also to be reemphasized that the parents should be instructed to remove all obvious sources of allergenic material from the child's immediate environment. Unfortunately, if it has not been done previously, this is sometimes difficult to accomplish during an attack with the general chaos that goes on in many families; also, moving things around will tend to stir up dust and mold spores in the bedroom. Therefore, the father is frequently told to take the child out for an automobile ride while the mother carries out specific elimination measures in the bedroom. This procedure also tends to break up some of the frequently coexisting emotional constellation.

Status Asthmaticus

If, in spite of proper early medication of an attack, or if one sees a more advanced attack for the first time, then one must proceed from milder medications in a step-wise fashion to more potent drugs. Soon after the initiation of an attack, if ephedrine and secobarbital fail to control it, then epinephrine (Adrenalin), both in aqueous solution and in oil, should be administered. Not infrequently, the parents are taught to administer epinephrine in the home. This gives them added confidence in their total ability to handle an attack, thus decreasing their anxiety and overconcern with the attendant potential deleterious effect. Instructions for the home administration of epinephrine must be given thoroughly and carefully with explicit directions as to amount and repetition before the physician is called. A practice may be made of actually drawing in the amounts of both preparations of epinephrine on printed facsimilies of syringes, which are given to the parents.

A word should be said about nebulizers containing epinephrine or other potent bronchodilating inhalants. I seldom prescribe these for a child, for in my experience they are all together too "handy" to use and I have observed that the child frequently tends to develop a great dependence on the use of this modality. When it is really needed, the "needle" for epinephrine will be resorted to, but it is much less likely to be promiscuously overused and, thus, the chance for development of epinephrine overdependence and/or "fastness" is lessened.

If bacterial infection is present, in either early or later stages, the child should receive adequate treatment with sulfonamides or a broad-spectrum antibiotic. I have not given a dose of penicillin during the past two years of practice to an allergic child and will not in the future unless an organism is encountered that is outside the spectrum of other acceptable parenterially administered antimicrobial agents. The reasons for the omission of this excellent antibiotic for the therapy of allergic children become more apparent almost monthly, with increasing reports of severe morbidity and of fatalities from its use in atopic individuals. Penicillin's widespread use, the relative frequency of Penicillium as an inhalant mold spore in many areas, presence of antigenically unmodified penicillin in milk from use by veterinarians in treating bovine infections, and its use as a preservative in vaccines have given many individuals a basic source of sensitization.

When antimicrobial therapy is carried out in the allergic child, it should be maintained to conclusion (including at least two afrebile days), for one must remember that it is not just the infection per se that should be treated but that the host may be hypersensitive to the type-specific protein of the invading bacterial organism.

Now, if infection is not present or is "covered," and if ephedrine, barbiturates, and epinephrine fail to almost completely block the attack for a period of over 48 hours, with the attack progressing to moderately severe intensity and poor fluid intake, then I believe that the potential damage to the child, both physically and emotionally, from his asthma outweighs the possible damage that could accrue from the proper use of steroid therapy. Therefore, in this situation, I then institute steroid therapy in what might be called a "hit-and-run" technique. The patient is given a calculated dose of ACTH (10 to 40 units), and adrenal cortical steroids are prescribed in amounts sufficient to block the attack. This dosage is decreased over a five-day period to a maintenance amount which is given for five more days. Adrenal steroids then are withdrawn, and the patient is given ACTH on the succeeding day to help stimulate the adrenal cortex, which some investigators believe is slightly depressed after even short-term corticoid therapy.

Should all these measures fail and the patient begin to show definite signs of dehydration, then hospitalization may be required. If the aforementioned procedures are followed, hospitalization for the asthmatic child is seldom indicated; rarely is it necessary for the child under therapy with a total antiallergic regimen.[5]

If hospitalization is required, only two gains are to be expected other than removal of the patient from an emotion-packed environment: (1) fluids given parenterally, and (2) oxygen, carbon dioxide, and mist via the tracheobronchial route. The former is accomplished effectively and without danger in infants and children only when a pattern of well-established methods of fluid restoration is followed. This has been delineated for the asthmatic child in a previous communication[2] and need not be reviewed here.

Inhalants and Expectorants

A few words must be said concerning the administration of oxygen and the use of expectorant drugs. The use of expectorants and cough mixtures is far more an art than a science. It has its origins in the earliest practice of medicine and is deeply rooted in the folklore and mumpsismus of medicine. Only in recent years, for the most part the past 15 or 20, has the problem of medication with expectorant drugs been the subject of objective laboratory and clinical investigation. The results of such investigations provide some support for the common expectorant drugs, though with respect to the use of ammonium chloride, for example, it is stated that "it is not unlikely that some of the action ascribed to ammonium salts is in reality due to the ingestion of water usually prescribed with cough medicine containing the salt."[6] When expectorants are used, however, iodides are usually preferred,[7] either in the form of potassium iodide or as syrup of hydriodic acid.

With respect to inhalants, however, much sound information is known, and on the basis of this information rests the proper use of oxygen, carbon dioxide, and steam. Among inhalants, steam and carbon dioxide have been found to be excellent expectorants. Steam or a very high relative humidity (above 85%) liquefies sputum, decreases its viscosity, and affords the patient considerable symptomatic relief. In a number of classic studies, carbon dioxide has been proved the most effective agent of all.[7] It not only lowers the viscosity of tenacious sputum, thereby facilitating expectoration, but decreases the volume of sputum by promoting its active resorption by the bronchial mucosa. In addition, this gas increases both rate and depth of respiratory movements and stimulates the cough reflex, actions which assist in evacuation of the contents of the more dependent regions of the respiratory tract. A 5-to-10% concentration of carbon dioxide is adequate and well tolerated if administered at intervals. The combination of steam, expectorant drugs, and carbon dioxide is especially effective. Oxygen has been shown to be an antiexpectorant and has effects opposite to those of carbon dioxide. When oxygen therapy is essential in cases in which its antiexpectorant action may be harmful, steam and carbon dioxide may be added to counteract the untoward effect on bronchial secretions.

Summary

Salient features in the therapy of acute attacks of asthma in infants and children include early bronchodilation, sedation, and hydration, and elimination of allergens. The physician must select a few drugs and learn their action well, both physiologically and from experience with their use. When it is necessary to utilize inhalant therapy, it must be used on sound physiological principles. In all, the physician must be cognizant of the emotional factors at play—both in the little patient and in the parents—and of their interaction.

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DERMOGRAPHIA—CLINICAL OBSERVATIONS

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Dermographia is commonly demonstrated by stroking the skin with a blunt instrument. The response is a local swelling and itching, and the itching is increased by anything that will cause vasodilation in the skin. Emotions sometimes contribute to the vasodilation. The reaction is sometimes immediate, sometimes delayed. Its relation to urticaria has been difficult to explain. The most effective remedies are the antihistamines, the choice and dosage being determined by the individual needs and tolerance of the patient.

Dermographia is the most common form of physical allergy. It is frequently diagnosed as chronic urticaria. In a large number of patients primary dermographia seems to be the only cause of urticaria. A dermographic basis is easily overlooked. Failure to consider dermographia can lead to misinterpretation of skin tests. This doubtless accounts for a patient's stating that his skin tests showed him to be "allergic to everything."

The purpose of this paper is to stimulate interest in a poorly understood but commonly seen condi-

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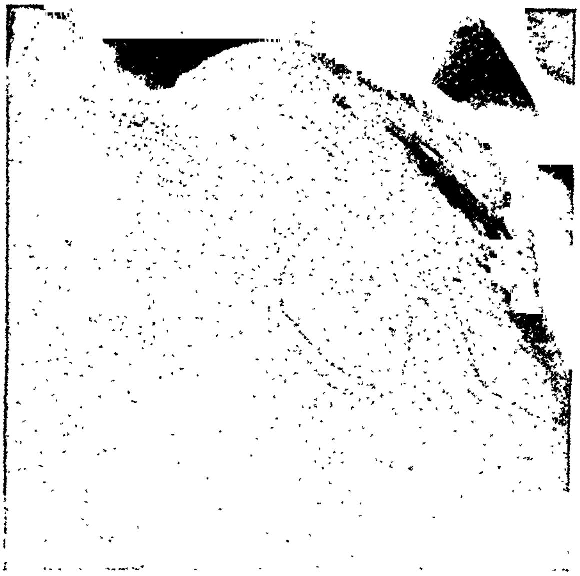
tion by relating our observations and opinions. A bibliography more extensive than the direct references may be obtained from us.

We define dermographia as a whealing response of the skin to trauma. This may be commonly demonstrated by stroking the skin with a blunt instrument, such as a paper clip, tongue blade, or fingernail (see figure). The chief symptom is itching. Occasionally, cases date from early childhood, with the skin response quite marked but with the patient complaining of very little pruritus. We have the impression that the incidence of dysmenorrhea, gastrointestinal symptoms, and headaches is increased in persons with dermographia. This is possibly due to the excess amount of histamine that seems to be present throughout the body.



Whealing response of skin to trauma.

Any condition that will cause vasodilatation in the skin will increase itching, which may explain the aggravation caused by blushing, taking a hot bath, or drinking large amounts of hot coffee or tea. Related terms are factitial, dermographic, and mechanical urticaria and autographism.

Review of the Literature

Gilchrist[1] reported the first case of dermographia in English literature in 1908, followed in 1912 by Eustis.[2] The famous monograph of Lewis[3] in 1927 on the "triple response" was an outstanding stimulus of interest in dermographia. There seems to have been a dearth of interest from 1935 to 1945. After the discovery of the antihistaminic drugs there was renewed interest. Unfortunately, some psychiatrists[4] writing on this problem stated that dermographia could be explained on a psychosomatic basis. Most of these psychiatrists seemingly have confused this condition with neurotic excoriation and factitial dermatitis.

Lewis[3] states that among young and healthy persons whealing of the skin as a consequence of firm stroking is not infrequent; a detectable swelling is found in about 25% of those tested. In about 5% a conspicuous wheal is produced. Some whealing in response to stroking is frequent, if not the rule, in children. In normal persons a red line appears within 3 to 18 seconds and reaches its height within 30 to 50 seconds after stroking. Whealing can be produced in almost any human skin by repeatedly stroking the same area.

Dermographia should be considered in every case of chronic urticaria. We disagree with Fisher and Schwartz[5] who, in 1953, stated that there was a low incidence of dermographia in patients with subacute and chronic urticaria. The incidence seems to have increased with the general use of penicillin. We have seen it follow reactions to horse serum, aspirin, codeine, sulfonamides, and, occasionally, poison ivy dermatitis.

The incidence of dermographia may be greater when atopy is present than when it is not. Since our practice is limited to allergy, we are not prepared to estimate the incidence among the general population. A familial or hereditary tendency has never been proved. We have treated a family in which both parents and four children had dermographia. Winkelmann[6] states that it may be familial.

Classification and Etiology

Classification.—We think of dermographia as being primary or secondary. Secondary dermographia is that following an intensely pruritic allergic reaction to drugs or contact dermatitis, while the primary form has no known cause. This is not to say that the drugs or contacted agents are directly responsible for the dermographic reaction. The latter is a response to trauma.

The reaction itself may be either immediate or delayed.[7] The immediate wheal is apt to be linear and lighter in color. Delayed reactions have a more inflammatory quality, with induration and a brawny appearance. They usually occur two to six hours after trauma. They disappear more slowly than the immediate type. The individual lesions are less apt to be linear. They are due more often to pressure than to scratching.

Etiology.—Duke[8] classified dermographia as a physical allergy. He failed to induce passive dermographia in a normal patient with 1,000 cc. of whole blood given intravenously from a patient with dermographia. Walzer[9] and Lehner and Rajka[10] were able to passively transfer dermographia. Our experience has been similar to Walzer's, in that in some patients we have been successful in transferring passive dermographic sensitivity and that it is of short duration (a few hours). We have obtained passive transfer reactions with use of fresh serum. However, after being left in the refrigerator for a week the same serum failed to sensitize the same receptor. Lewis and Grant[11] showed that the wheal produced by stroking in dermographia is identical to the wheal produced by histamine in nonallergic subjects.

We believe that emotions are important only as contributory factors due to the accompanying vasodilatation. Rothman[12] states that wheal formation is independent of the nervous system and, therefore, on physiological grounds it is doubtful that urticarias (and dermographia) are of primary psychogenic origin. He also states that histamine liberated from the mast cells of the skin is the final event.

The exact roles of acetylcholine, heparin, and serotonin (5-hydroxytryptamine) in the cause of dermographia have never been determined. Until proved otherwise, the histamine concept of the cause must be accepted at least partially. Feinberg and Durham[13] believe that the condition is allergic, as the mechanism can be temporarily exhausted by repeated mechanical stimulation.

Pressure urticaria is probably a form of dermographia. Patients offer complaints of itching and hives at such sites of pressure as belts, suspenders, shoulder straps, brassieres, garter belts, girdles, corsets, and waist bands. Edema response is, at times, evident in the deeper tissues. These patients have swollen feet after long periods of standing. The hands may swell and feel stiff and even painful after mowing the lawn or driving. We have seen massive edema of the buttocks in patients with dermographia who sat for long periods of time on hard benches.

Vallery-Rodot reported one case of dermographia that affected the mucosa. Dermographic response frequently extends to the synovial membranes. We have noticed this more in drug-induced dermographia. It also seems at times to extend to the mucous membranes, so that physical irritation, such as ground dust, laughing, and unusual exertion will cause asthmatic breathing.

One patient, a 20-year-old man, was first seen for hay fever and also was found to have marked dermographia. One year after the first examination he showed typical lesions of atopic dermatitis at the waist and other friction areas. A similar case occurred in an obese 30-year-old woman with lesions under her shoulder straps. These were due not to rubber but to pressure, repeated scratching, and rubbing.[14]

In our opinion, patients who state that they are "allergic to wool" frequently have dermographia, and their sensitive skins are irritated by the rough fibers of the wool. Patch tests for allergy to pure wool and to the wool in question showed negative findings in every case. In girls, wearing a cotton blouse under the wool sweater has solved the problem.

Treatment

The antihistamines are effective if given in adequate doses. It is important to find an antihistaminic drug that the patient will tolerate without side-reactions and that, at the same time, will be effective. Chlorcyclizine hydrochloride (Perazil), given in a dosage of one or two 50-mg. tablets every 8 to 12 hours, seems to be most generally successful in our hands. Long-acting chlorpheniramine (Chlor-Trimeton) maleate and tripelennamine (Pyribenzamine) hydrochloride tablets seem to work better in certain cases. Pyrrobutamine compound (Co-Pyronil) is effective at times. Epinephrine (Adrenalin) in a 1:1,000 aqueous solution given subcutaneously is rapid and effective in its action. Diphenhydramine (Benadryl) hydrochloride often is useful at bedtime, as it encourages sleep. Some of these patients may need maintenance antihistaminic therapy for a long period of time.

At times the steroids, including prednisone and prednisolone, seem to aggravate the condition. The same applies to corticotropin (ACTH). We do not advocate their use in the treatment of dermographia.

We have not tried the "histamine liberators," such as compound 48-80 (a condensation product of *p*-methoxyphenylethyl-methylamine and formaldehyde), or Bol 148 (2-bromo-d-lysergic acid diethylamide), the antagonist of serotonin. A histamine azoprotein (Hapamine) is valueless in our opinion. Pilocarpine nitrate, in doses of 5 mg. (1/12 grain) was said to be of help in a few patients treated some years ago.

Penicillinase (Neutrapen), in our experience, has not been successful in the treatment of patients with dermographia after serum sickness reactions from penicillin. Patients have complained bitterly of pain at the site of the injection, and one patient had a large swelling with a fever of 102 F (38.8 C) for 24 hours. Another patient had an anaphylactic reaction after the second dose of penicillinase given eight days after the first.

Patients should be instructed that dermographia is disagreeable rather than dangerous. They should be assured that it is not a manifestation of any organic disease, that there are no serious complications, and that the condition is usually self-limited. They can usually be made comfortable with inexpensive and non-habit-forming medicaments, such as antihistamines.

Summary

Dermographia is a common clinical entity and is the most common form of physical allergy. It is frequently overlooked, but it should be considered in any case of unexplained chronic urticaria. The incidence seems to be increasing. An allergic response to penicillin frequently leaves the patient with long-standing dermographia. Antihistamines are generally effective in the relief of this condition.

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CLINICAL AND METABOLIC STUDY OF CHLOROTHIAZIDE (DIURIL)

USE IN EDEMA OF NORMAL PREGNANCY AND OF TOXEMIA OF PREGNANCY

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The diuresis induced by chlorothiazide (Diuril) was studied in 15 patients hospitalized for toxemia of pregnancy, 100 women whose pregnancies were progressing normally, except for varying degrees of pitting edema of the legs, and 35 additional patients in whom the edema, being complicated by hypertension with or without proteinuria, led to the diagnosis of toxemia of pregnancy. Doses of 500 mg., one to four times daily, resulted in striking increase in the urinary excretion of sodium and chloride ions and of water, with corresponding loss of body weight. Potassium excretion was also increased, but not so strikingly, and the excretion of ammonia and titratable acids was less significantly affected. The intravenous administration of 5 to 10 mg. of chlorothiazide per kilogram of body weight caused similar diuresis beginning within 20 minutes after the injection, without any significant effect on blood pressure and pulse rate. The data showed that chlorothiazide can be used with satisfactory results and with minimal side-effects in the treatment of edema of pregnancy.

Although the etiology of acute toxemia of pregnancy is still unknown, it is generally agreed that edema is one of the most constant and early manifestations of the disease. It is also common knowledge that the clinical manifestation of edema is not limited to toxemia of pregnancy but is also frequently found in normal pregnancy. It is estimated that from 30 to 40% of normally pregnant women have varying degrees of edema, particularly after the fifth or sixth month of gestation. It is, therefore, essential to differentiate this type of edema from that existing in borderline cases of toxemia of pregnancy, a task which is often quite difficult. Nevertheless, a salient difference between the two forms of edema is that the edema of normal pregnancy remains limited to the lower extremities and usually subsides rapidly when the patient remains at bed rest or merely restricts salt intake, whereas the edema seen in toxemia of pregnancy is usually more generalized. The latter often presents as edema of the hands and face, as well as of the lower extremities, and its control usually demands a more stringent and therapeutic regimen than merely bed rest and dietary salt restriction.

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Not only do these two forms of edema differ in clinical manifestations and response to therapy but the physiological etiology of each appears to be different also. Recent, as yet unpublished, work in our laboratories has suggested that the edema of normal pregnancy may be related to increased sodium reabsorption by the renal tubules, this being invoked by stimuli acting on volume receptors located in various areas of the left side of the heart. These centers are probably activated by pooling of blood in the lower extremities, occurring when the pregnant woman assumes a standing position.

Evidence has been accumulated which shows that the edema in toxemia of pregnancy is caused by increased reabsorption of water and electrolytes by the renal tubules. The initial stimulus for this increased reabsorption of water and electrolytes is still in dispute, but two main theories have been advanced. The first theory attributes electrolyte retention in toxemia to a decrease in glomerular filtration rate, a state which undoubtedly exists in the majority of patients with toxemia. This decrease in filtration rate will then result in a decreased filtered electrolyte load, thus producing a disturbance in the glomerular-tubular balance, and the tubules will then be stimulated to reabsorb more electrolytes for a given load.

The second theory states that the increased sodium reabsorption by the renal tubules may be related to increased secretion of mineralocorticoid hormones by the adrenal cortex. Several investigators have shown that the urinary excretion of these hormones is somewhat elevated in patients with toxemia of pregnancy. However, since a similar increase has also been observed in normal pregnancy and because the patients studied were on diets with restricted salt intake, it is difficult to evaluate the contribution these hormones make to the water and electrolyte retention in toxemia. Therefore, at present it is difficult to determine whether the excretion of aldosterone is the cause or the result of toxemia.

Despite our ignorance as to the primary cause of edema in toxemia of pregnancy, the fact remains that this clinical abnormality is so frequent that its clinical management becomes essential. Various drugs have been used in the management of edema of normal and abnormal pregnancy. A detailed review of the subject has been recently made by one of us,[1] and the reader may refer to it for further information.

The present report deals with the reaction and clinical use of a new therapeutic agent, chlorothiazide (Diuril), in the treatment of edema of normal pregnancy and of toxemia of pregnancy. Chlorothiazide was synthetized recently by Novello and Sprague [2]; they, with Beyer and co-workers,[3] were also the first to report on its therapeutic properties. Pharmacological studies in animals and humans have shown that the oral administration of the drug produces a marked increase in urinary excretion of sodium, chloride, and, to a certain degree, potassium. While in vitro this agent seems to have an action which resembles the carbonic anhydrase inhibitors, in vivo, in the doses clinically used, this action is not strikingly evident because the bicarbonate levels in blood and urine, which are the main targets of carbonic anhydrase inhibitors, are not affected by chlorothiazide. The main targets of this drug are the chloride and sodium ions, although when intravenously given the drug may also increase the excretion of bicarbonate.

Material and Methods

Metabolic studies of orally and intravenously given chlorothiazide were carried out on 15 patients with toxemia of pregnancy who were in the hospital at bed rest and without any specific medication. Each patient received a diet containing 85 mEq. of sodium as sodium chloride. The studies comprised three consecutive periods. The first period lasted from three to five days and served as a control period. This was immediately followed by a second period lasting from four to six days in which chlorothiazide was given orally in a quantity totaling from 500 to 2,000 mg. per day in two or three divided doses. The third period served as a recovery period and lasted for three to five days.

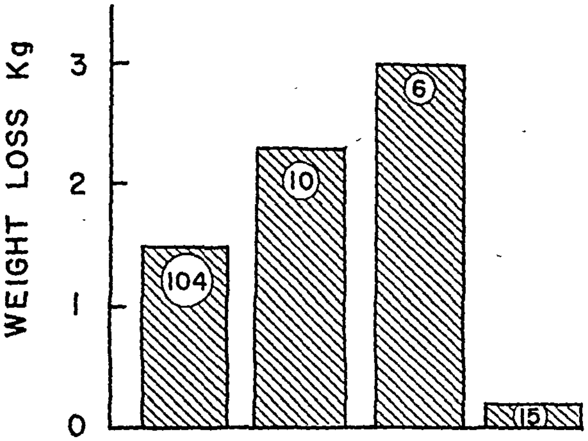
During each period the patient's weight, blood pressure, intake, and output were recorded. Blood samples were obtained daily for analysis of electrolytes, pH, and carbon dioxide. Twenty-four hour urine specimens were collected and served for the analysis of electrolytes, ammonia content, and titratable acids. Some patients were studied on two periods of chlorothiazide treatment alternated with recovery periods. This was done in order to test the efficacy of repeated courses of chlorothiazide treatment. One patient was studied while she was on a diet containing 8.5 mEq. of sodium. This was done in order to test the action of the drug in patients who are on diets with salt restriction.

The effects of intravenous administration of chlorothiazide on water and electrolyte excretion, as well as on renal hemodynamics, were studied by giving the patient, intravenously, doses of 5 to 10 mg. per kilogram of body weight. Three to four clearances of inulin and para-aminohippuric acid were measured as controls, and four to five determinations were made after the intravenous injection of the drug. Blood and urine samples were analyzed for their content of sodium, potassium, chloride, inulin, para-aminohippuric acid, and carbon dioxide by methods in current use in our laboratories.[4]

In addition to the metabolic studies, clinical observations were carried out on 135 pregnant patients who were examined in the prenatal clinics. Of these, 100 were classified as having normal pregnancy, but with edema of the legs varying from 1+ to 4+. Although these patients had definite pitting edema and rapid weight gain, none of them exhibited the other signs of toxemia, namely, hypertension and proteinuria. The other 35 patients had, in addition to edema, varying degrees of hypertension and, in some instances, proteinuria. These patients were classified as having toxemia of pregnancy. The criterion for the efficacy of the drug in all these patients was the change of weight. Patients were weighed once every week before, during, and after treatment. Care was observed to have the patient wear the same clothes during the examination, and the weight was always checked at the same time of day. The drug was administered to these patients orally in a standard dose of 1,000 mg. divided in two doses per day, and treatment was given for periods of five days interrupted by two to three days of drug-free periods.

Results

General Effects.—All the patients tolerated the drug well. No side-effects were observed, and in no instance was the drug withdrawn because of signs of intolerance. Irregular variation of blood pressure was observed in the patients with hypertension, but this variation could not be attributed to the drug action.



Average weight loss in 135 patients who received chlorothiazide for five days (circled numbers refer to number of patients).

Metabolic Effects.—Details of the metabolic studies have been published elsewhere.[4] Oral administration of chlorothiazide resulted in striking increase in the urinary excretion of sodium and chloride. Maximum increase occurred on the first and second days of therapy, and levels decreased progressively on subsequent days until the last day of treatment. Potassium excretion also increased after the drug administration, but the increment in the excretion of this ion was less striking than those of sodium and chloride.

Concomitant with the increase in electrolyte excretion was an increase in urine output and loss of weight. The excretion of ammonia and titratable acids was not significantly affected. In some patients, plasma electrolyte levels, particularly those of chloride and potassium, fell, while in others they remained unchanged. On cessation of therapy, a marked retention of electrolytes occurred but the amount retained was below that excreted during the administration of the drug.

Effect of Intravenous Administration.—Intravenous administration of chlorothiazide in doses varying from 5 to 10 mg. per kilogram of body weight did not change the blood pressure, renal plasma flow, or glomerular filtration rate. However, the excretion of sodium and chloride strikingly increased within the first 20 minutes after the injection of the drug. Although in subsequent collection periods the effect decreased somewhat, the excretion of these ions remained high throughout the entire experiment. The excretion of potassium also increased, as did the excretion of water, but in both instances the increment was less significant than that of electrolyte. Total solute excretion was markedly elevated after the injection of the drug. The intravenous administration of the drug did not have any significant effect on the blood pressure and pulse rate.

Clinical Observations.—Of the 135 patients seen in the prenatal clinic, 104 had an average weight loss of 1.5 kg. (3½ lb.) after the first week of treatment with chlorothiazide; 10 patients lost an average of 2.25 kg. (5 lb.) and 6 lost approximately 3 kg. (6¾ lb.). The remaining 15 had insignificant loss of weight during the first week (see figure).

Comment

Our present data show that chlorothiazide given by the oral or intravenous route to patients with normal pregnancy or to patients with toxemia of pregnancy increases primarily the excretion of sodium, chloride, and potassium and secondarily the excretion of water. Its site of action appears to be the renal tubule, although the exact mechanism of action has not been properly understood. It is postulated that the drug acts by inhibiting the reabsorption of these ions by the renal tubules.

The drug, in vitro, is a potent carbonic anhydrase inhibitor, but, when given orally, it does not seem to have any action which would suggest carbonic anhydrase inhibition. However, when the drug is injected intravenously there appear to be definite signs of carbonic anhydrase inhibition, manifested by a certain degree of acidosis and a marked bicarbonate loss.

It should be realized, however, that the action of this drug is far more complex than is implied, since, despite its apparent carbonic anhydrase inhibition, it still increases the excretion of chloride, a property not possessed by other true carbonic anhydrase inhibitors.

The diuretic action of chlorothiazide, when given orally, is prompt and reaches its maximum on the first day of treatment. When injected intravenously, maximum effect is observed within the first 30 minutes. In either instance, the effects of the drug become progressively less, even though in a number of cases some diuretic action was still present after the fifth day of treatment. One may hypothesize that the answer for the decreasing diuretic effect is either that a tolerance to the drug develops, which is unlikely, or that, in the patients to whom the drug was given, the stores of electrolytes and water available for excretion are somewhat limited. This hypothesis receives further support from the metabolic studies performed on patients with low sodium intake. In these patients, the effect of the drug is transitory and the increment in the excretion of sodium and chloride may not last more than one day. In these patients, chlorothiazide may deplete rapidly body electrolyte levels and, if this is not corrected, lead to hypokalemic hypochloremic alkalosis.

Orally given, the drug seems to have a flat dose-response relationship curve, since the effects of a 2,000-mg. dose were not significantly different from those of a 500-mg. dose. (Just whether higher or lower doses than those utilized in these studies would have different effects cannot be stated at the present time.) However, it is felt that the data indicate that satisfactory results with minimal side-effects can be achieved with any dose within the 500-mg. and 2,000-mg. range.

The absence of any significant action on blood pressure is in disagreement with some reports on the effects of this drug in patients with hypertensive conditions. A possible reason is that, in our studies, chlorothiazide was given alone and the period of observation was relatively short.

The retention of water and electrolytes which invariably occurs after cessation of chlorothiazide therapy is peculiar to all diuretic agents. It seems to represent a compensatory homeostatic mechanism on the part of the organism to restore a part of the electrolytes lost during diuresis. Nevertheless, this action should not preclude the use of this agent to remove edema, since the quantity of electrolytes retained in the recovery period is significantly smaller than the increment excreted during therapy.

Summary and Conclusions

Clinical and metabolic studies of chlorothiazide (Diuril) were done in patients with normal pregnancy and in those with toxemia of pregnancy. The drug increases markedly the excretion of sodium and chloride and, to a lesser extent, potassium and water. Given intravenously, the drug exhibits certain properties of carbonic anhydrase inhibition. It is less effective in the nonedematous subjects, particularly when sodium intake is restricted. In some of these patients, depletion of body electrolytes may occur. Given orally, the drug seems to be effective in the majority of ambulant patients with edema. The effective dose is between 500 and 2,000 mg. per day.

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CHANGING FACTORS IN DISEASE.—Our bodies are complicated built-in chemical laboratories, evolved ages ago under primitive conditions. Already we are discovering disquieting facts. Longer life span is being purchased at the cost of increasing numbers of the aged whose survival creates new problems. . . . Not merely is mastery of existing diseases incomplete; germs and viruses are learning to thrive on drugs which, a year or two ago, were fatal to them. The history of past epidemics is a tragic story. . . . It may be thought that, as we now understand carriage of disease by lice, fleas, contaminated water, flies, rats and mosquitoes, the history of past epidemics has but slight significance. Such thinking is of the ivory castle brand. Life is never static. We are losing resistances to certain germs, and germs are evolving in their race for survival. Owing to their extraordinary rate of reproduction, the possibilities of a new variety by mutation is very real. The delicate balance between immunity and disease may be tipped against us. The rapidity of international travel fosters air-borne and contact dissemination of disease on a world scale and is creating a situation which may be difficult to control. We would indeed be well advised to continue to read and disseminate the history of epidemics as a spur to continued vigilance in the field of public health.—J. Bostock, M.D., Medicine's Need for History, *The Medical Journal of Australia*, Oct. 25, 1958.

CLINICAL NOTES

ANALYSIS OF THE PRECIPITATION TEST FOR SYSTEMIC LUPUS ERYTHEMATOSUS

Carl M. Pearson, M.D., Los Angeles

Within recent months, there was reported in The Journal[1] the results of a simple serum precipitation test which was frequently found to be positive in patients with systemic lupus erythematosus and rarely reactive in most other conditions. The first details of this test were verbally presented in June, 1957,[2] after which the test was performed on a number of the patients from the wards and clinics of local medical centers in the Los Angeles area. Equivocal or contradictory results were often found in these patients, and, hence, the test as a routine procedure was discontinued in the fall of 1957. After the publication by Jones and Thompson[1] of their results with this procedure, it was carefully and systematically reevaluated in most of the original patients as well as in many new ones, including a number of unselected hospitalized patients who had a wide range of medical diseases, both minor and major.

The selection of cases in addition to those of systemic lupus erythematosus has emphasized the inclusion of a large representation from the various rheumatic and connective tissue disease categories, since it is from these groups that the differentiation of systemic lupus erythematosus is often most difficult and it is where a simple laboratory test that could set apart this disorder from its close associates could prove its worth.

This report is a survey of 221 tests made on 183 persons with various rheumatic and connective diseases, including 41 tests on 25 patients with systemic lupus erythematosus and 58 single tests in persons with various medical diseases. As will be pointed out, the specificity of the test for systemic lupus erythematosus has not been confirmed. However, it is certainly true that a positive result is more likely to be found in a patient with one of the connective tissue disorders than in one with any of a variety of miscellaneous disease states and presumably also in the healthy population.

Procedure and Technique of Recording

The test solution was 12% *p*-toluenesulfonic acid in glacial acetic acid. All tests were done on serum. Many were performed on fresh specimens, but a number of serum specimens had been frozen at -20 C for various periods and were thawed immediately prior to testing.

Several specimens were tested in the fresh state and then repeatedly frozen and thawed and tested over a period of several weeks. In a few of these serum specimens variable and unexplainable results were obtained, so that serum that originally gave strongly positive results would give a weak result after one or more thawings and then revert to a positive result on another occasion. Most of the serum, however, retained the original positivity or negativity throughout the test period. No serum that was originally negative was observed to show a positive result after freezing and thawing. All tests were done by one person who had no prior knowledge of the patient's disease.

The performance of the test and the technique of recording were nearly identical to that originally set down by Jones and Thompson.[1] These procedures were repeated as follows: 0.1 ml. of serum was placed in a test tube and 2 ml. of the *p*-toluenesulfonic acid solution was pipeted down the side of the tube. The tube was shaken, allowed to stand for 20 minutes, and then reshaken. The result was recorded as follows: 1. If no clot or precipitate was seen after the addition of the test reagent or if it disappeared on shaking, the finding was read as negative. 2. If a precipitate persisted for 20 minutes after the original shaking but disappeared on reshaking, the recording was 1+. 3. If any precipitate remained after reshaking and standing for an additional 20 minutes, it was 2+. 4. If the precipitation at this time was moderate, it was termed 3+. 5. If the precipitate appeared as a heavy mass, it was recorded as 4+. For further reference and statistical treatment in this study, a result has been considered to be positive only with a precipitate graded 2+ through 4+.

Results

As recorded in table 1, 221 serum specimens were tested in 183 persons with various forms of rheumatic and connective tissue disorders, including gout. All of the patients have been seen in this hospital or its medical clinics, and details of their illness were well documented.

Twenty-five patients with systemic lupus erythematosus were carefully and often repeatedly tested over a period of several months. All had the disease as substantiated either by the presence of L. E. cells in the past or present or, as in four, by history and autopsy evidence of renal and other characteristic anatomic findings of this disease. In

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only six of these persons (25%), even on repeated testing, could a positive result be found. Since multiple tests were made on a number of these patients, the over-all positivity result was 27% of 41 serum specimens examined. Close correlation could not be drawn in this group of patients between the severity of the clinical state and the results of the test. Many were on steroid medication when tested, but those that were not did not show any higher incidence of positive results. The most rigid criterion of severity of the disease state is, of course, a fatal termination. Six persons in this series died of systemic lupus erythematosus, and renal failure was the chief cause of death in three. From a total of 14 serum specimens obtained over a period of weeks or months in this group of six seriously ill persons, not a single positive result was recorded. Four of these serums from separate patients were tested prior to steroid therapy.

TABLE 1.—*Results of Precipitation Test in Patients with Various Rheumatic and Connective Tissue Disorders*

Disease	Cases, No.	Specimens, No.	Results, No.					Positive Results (2+ to 4+), %
			0	1+	2+	3+	4+	
Systemic lupus erythematosus	25	41	22	8	5	1	5	27
Rheumatoid arthritis	94	100	48*	20	19	7†	6	32
Rheumatoid spondylitis	13	15	5	2	7	1	0	53
Discoid lupus erythematosus	4	4	2	1	1	0	0	25
Scleroderma	5	5	0	1	2	1	1	80
Polymyositis and dermatomyositis	11	22	12	1	4	3	2	41
Vasculitis, type unclassified	5	7	3	1	2	1	0	43
Reiter's disease	3	3	1	2	0	0	0	0
Osteoarthritis	11	11	8	1	2	0	0	18
Gout	8	9	3	1	3	1	1‡	56
Fibromyositis	4	4	2	1	0	1	0	25
Total	183	221	106	39	45	16	15	35

* 1 case of periodic hydrarthrosis.
† 1 case of juvenile rheumatoid arthritis.
‡ This patient also had active duodenal ulcer.

The largest single group of persons tested were those with rheumatoid arthritis. One hundred tests were made on 94 patients with various grades of active rheumatoid disease. Thirty-two per cent gave a positive result. Again, a significant correlation could not be drawn between the extent of the clinical disease or its degree of activity and the positivity of the test. In a smaller group of persons with rheumatoid spondylitis, 53% of the tests gave positive findings. The remainder of the results have been recorded in table 1. Of particular note is the high incidence of positive results in a small group of persons with scleroderma and in another group with gout. The patients with polymyositis and those with an ill-defined disease showing biopsy evidence of vasculitis also more frequently showed a positive result than did the patients with systemic lupus erythematosus.

TABLE 2.—*Results of Precipitation Test in Various Nonrheumatic Medical Diseases*

Cases, No.	Results, No.					Positive Result (2+ to 4+), %
	0	1+	2+	3+	4+	
58	42	9	3*	3†	1‡	11

* 1 osteomalacia; 1 duodenal ulcer; 1 Raynauds' disease.
† 1 cirrhosis; 1 acute hepatitis; 1 active tuberculosis.
‡ 1 myelogenous leukemia.

Among 58 hospitalized persons with a wide variety of nonrheumatic medical disorders, 7 (11%) showed a positive result. An analysis of these results and a list of the positive reactors are shown in table 2. In this group were included eight patients with generalized arteriosclerosis, seven with duodenal ulcer, four with diabetes mellitus, three with hepatic cirrhosis, and two with acute hepatitis and jaundice.

During the several months that this test has been done, a number of patients have been repeatedly examined and many bizarre and unpredictable results were observed. It has not been possible to correlate, with any degree of certainty, the clinical status with the degree of positivity of the serum test, nor has cortisone favorably affected the test findings, even though the clinical condition has often seemed to have improved with this medication.

In table 3 are shown the results of serial examinations on five patients and the time span over which the serum was tested. The patient in case 1 had systemic lupus erythematosus manifested chiefly by thrombocytopenia. Prednisone therapy was started between the taking of specimens 1 and 2, and striking clinical improvement soon occurred, which persisted with continued steroid medication. Despite this, the precipitation tests have ranged from 0 to 4+ over a three-month period. The patient in case 2 had severe systemic lupus erythematosus with multisystem involvement and yet, by the designated criteria, has not shown a positive test result. Specimens 1 and 2 on this patient were obtained prior to steroid medication. The patient in case 3 had active rheumatoid arthritis with persistent multiple joint effusions. He was treated with intra-articular administration of hydrocortisone, salicylates, and conservative measures. There has been no visible evidence of clinical remission in his disease process, and yet the serial test results have shown a range of 0 to 4+. The patients in cases

4 and 5 were both women who suffered from an inflammatory muscular disease termed polymyositis. Both have been on continuous low-dosage steroid medication, and each has shown moderate and progressive clinical improvement. The most recent test result in each of these cases was 4+.

Comment

It would be impossible to conclude from any form of analysis in this series of patients that the *p*-toluenesulfonic acid serum precipitation test is at all specific for systemic lupus erythematosus. It does appear, however, that the test result is much more likely to be positive in patients with one of the rheumatic diseases (35%) than in those with a variety of nonrheumatic medical disorders (11%). Exceptions to this rule may be those persons with severe hepatic dysfunction and with various forms of dysproteinemia. The difference does not, however, render the test of great diagnostic value, since, as was recently pointed out by Lee and Schultz,[3] the pattern of observed reactions between rheumatic and nonrheumatic disorders is similar to and as nonspecific as those in the C-reactive protein, serum mucoprotein, thymol turbidity, cephalin-cholesterol flocculation, and other similar procedures.

TABLE 3.—*Serial Serum Precipitation Test Results in Five Patients*

Case, No.	Sex	Age, Yr.	Disease	Results of Test 1	2	3	4	5	6	7	Time Span for Obtained Specimens, Mo.
1	F	26	Systemic lupus erythematosus	3+	1+	2+	2+	0	4+	...	3
2	M	16	Systemic lupus erythematosus	0	0	1+	0	0	1+	0	10
3	M	54	Rheumatoid arthritis	1+	4+	0	2+	0	...	...	7
4	F	26	Polymyositis	0	1+	3+	0	0	3+	4+	7
5	F	39	Polymyositis	0	3+	2+	0	4+	...	...	8

No effort has been made in this study to attempt to identify the substance or substances responsible for the precipitation reaction, and at present the basis for the test remains indefinite.

There is general agreement between findings in the series of patients with systemic lupus erythematosus studied by Jones and Thompson[1] and the present series. When the criterion for a positive test is placed at a response of 2+ to 4+, in the former groups 40% of 30 tests are found positive and in the present 27% of 41 tests (on 25 patients). There is also some agreement between findings in the two series when patients with rheumatic and nonrheumatic diseases are compared in an over-all survey. However, there is significant and, at present, unexplained disagreement on the following points: 1. The severity of clinical systemic lupus erythematosus did not correlate closely in the present series with the positivity of the test result. 2. Steroid medication did not markedly affect a trend in the test result. 3. Most impressively, a positive result in the present series was no more likely to develop in a patient with systemic lupus erythematosus than in most patients with other rheumatic and connective tissue disorders. In six of these other diseases, in fact, the incidence of positivity was greater than that found in systemic lupus erythematosus.

In almost complete agreement with findings in the present series are the results of a similar study on 112 patients as presented recently in a brief notation in THE JOURNAL by Lee and Schultz.[3] In their group of 18 patients with systemic lupus erythematosus (25 tests), 52% of the findings were positive and in various other rheumatic diseases 60% were reactive. Also, in several persons with nonrheumatic dysproteinemia, 75% showed a positive result. Again similar to the present results is 16% positive findings in a group from which persons with rheumatic and dysproteinemic disorders were excluded.

The solitary laboratory criterion available at the present time for the diagnosis of systemic lupus erythematosus remains the L. E. cell test,[4] with the modifications recently devised to detect the abnormal circulating protein responsible for this phenomenon.[5] Possibly in this category also come the various serologic reactions which are being observed to develop in the serum of some persons with systemic lupus erythematosus when it is placed in contact with leukocyte products, including nucleoprotein and desoxyribose nucleic acid.[6] Less specific but strongly suggestive is the presence of chronic biological false-positive results in serologic tests for syphilis[7] or of a bizarre circulating anticoagulant and tissue biopsy evidence of perivasculitis, hematoxylin bodies, and certain renal or splenic vascular lesions. Other specific tests would most certainly be welcome. Unfortunately, the results obtained in the study of the present series of cases do not indicate that the *p*-toluenesulfonic acid test is of a sufficient degree of specificity to separate systemic lupus erythematosus from a variety of often closely related rheumatic and connective tissue disorders.

Summary

A recently reported serum precipitation test, with use of *p*-toluenesulfonic acid as the test reagent, has been studied, often repeatedy, in 182 persons with various rheumatic and connective tissue disorders and in 58 patients with various nonrheumatic medical diseases. There was a threefold greater incidence of positive results in the rheumatic than in the nonrheumatic group. The specificity of this test for systemic lupus erythematosus as opposed to other of the rheumatic ailments has, however, not been confirmed. In fact, in six other rheumatic diseases in this series the incidence of positive results was greater than in lupus erythematosus.

It is concluded from the pattern of observed reactions that the test is not specific for any disease state but rather is an obscure serum reaction with a specificity approximating that of the C-reactive protein, serum mucoprotein, and similar test procedures.

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Mr. Douglas Lawson performed all the tests in this study.

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EVALUATION OF A NEW ORAL RESUSCITATOR FOR EXPIRED-AIR ARTIFICIAL VENTILATION

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In view of the recent evidence that "mouth-to-mouth" and other forms of expired-air resuscitation are the most effective methods of artificial ventilation, an evaluation of the Venti-Breather oral resuscitator has been performed.

Studies recently performed by Gordon and coworkers,[1] Elam and others,[2] and Greene and coworkers [3] have shown that expired-air resuscitation is the only technique assuring adequate ventilation in all cases. In view of this fact, it would be of value if the public were encouraged to accept this type of resuscitative procedure as one of the methods for adults as well as for children.

Methods of Study

The valve was first evaluated for durability. It was made to perform during 36 hours of continuous operation under simulated operating conditions. The inhaling side was attached to an intermittent flow source of humidified compressed gas. A test-lung was attached to the exhaling side, simulating resistance of the average patient. On conclusion of 36 hours of continuous operation, there was no detectable damage or alteration of operating ability.

In evaluating the ventilatory adequacy of the unit for resuscitative purposes, arterial carbon dioxide and oxygen content were used as the criteria of adequate alveolar ventilation. These were determined by the manometric technique of Van Slyke. This is valid providing gas exchange between blood and pulmonary alveoli is not impaired.

The following procedures were employed: Five adult patients exhibiting no evidence of pulmonary or cardiovascular disease, who were scheduled for minor operative procedures, were chosen as subjects. All blood samples were drawn in oiled syringes containing heparin. The syringes were immediately capped with mercury and placed in ice. They were sent as quickly as possible to the laboratory for determination of arterial carbon dioxide and oxygen content.

After light premedication with an opiate and scopolamine hydrobromide or atropine, a Cournand needle was introduced into the brachial artery with the patient under local anesthesia. A control blood sample was obtained. Then the patient was given a sedative dose of thiopental (Pentothal) sodium and paralyzed with intravenously given succinylcholine chloride. A period of apnea, one and one-half minutes long, was then allowed to supervene. This was done in order to provide blood and alveolar carbon dioxide concentration higher than that found normally. Concomitantly, this resulted in a decrease in alveolar and arterial oxygen concentration. This period of apnea produced a trend toward the arterial carbon dioxide and oxygen content found in asphyxiated subjects without endangering the patient. A second arterial blood sample was then

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drawn as before. After this period, artificial ventilation was instituted by means of the Venti-Breather oral resuscitator. After two minutes of ventilation, a third arterial sample was collected. Ventilation was then done for eight more minutes in this manner, at the end of which time a fourth arterial sample was drawn and analyzed for oxygen and carbon dioxide content.

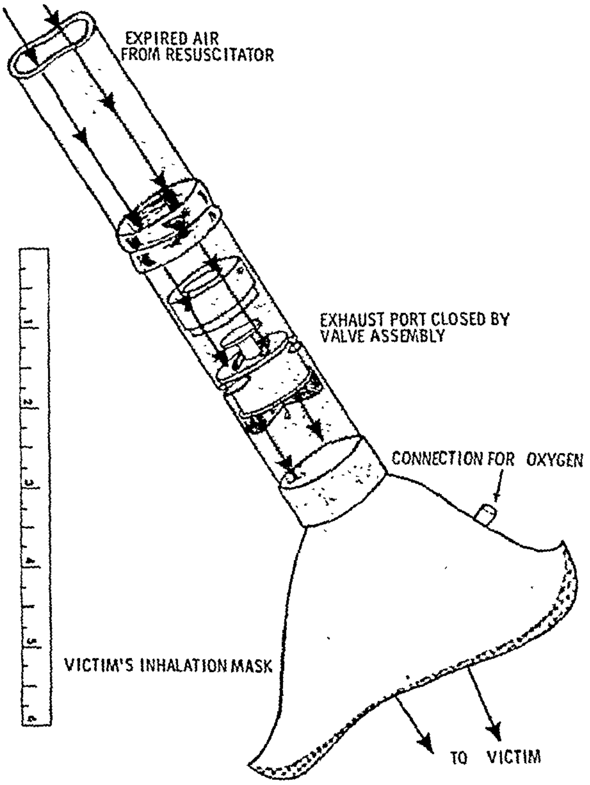
EXPIRED AIR FROM RESUSCITATOR
EXHAUST PORT CLOSED BY VALVE ASSEMBLY
CONNECTION FOR OXYGEN
VICTIM'S INHALATION MASK
TO VICTIM

Fig. 1.—Inhalation phase of resuscitator unit.

Results

In all instances, the arterial carbon dioxide and oxygen content after two minutes of expired-air ventilation with the Venti-Breather unit was near control levels. Average values were 16.5 vol. % for oxygen and 44.0 for carbon dioxide (control, 18.0 and 40.6 vol. % respectively). This was in contradistinction to those obtained after one and one-half minutes of apnea: 8.0 and 48.0 vol. % respectively. These values remained satisfactory in the 10-minute sample, when the average oxygen level was 17.7 vol. % and carbon dioxide, 38.7 vol. %. This would indicate that adequate alveolar ventilation had been performed in all subjects by the expired-air resuscitation technique with use of this valve.

Airway pressures delivered by this valve were determined by the insertion of a polyethylene tube, 4 mm. in diameter, in a leak-free manner through an opening in the side of the valve unit. This tube was placed under the mask via the nasal route into the trachea and connected to a U-tube mercury manometer. The average inspiratory pressure obtained was 12 mm. Hg; the average expiratory pressure was 0.

Airway pressures were not correlated with tidal volume. However, the patients' chest cages were well expanded in all instances.

Comment

The development of the Venti-Breather oral resuscitator is a step toward obtaining public acceptance of expired-air resuscitation. It eliminates the necessity for direct mouth contact, thus rendering the procedure esthetically more acceptable. After the resuscitator inflates (fig. 1) the patient's exhalation occurs through a one-way valve (fig. 2). This obviates the need to remove the resuscitator's mouth from the patient during the patient's exhalation and increases the effectiveness and ease of the procedure.

The unit is compact, simple, and easy to use. It can be used by itself or in conjunction with accessory equipment, such as additional face masks, oral airways, and endotracheal tubes. For these reasons, it, or a similar device, appears to be of potential value as an addition to the armamentarium of "first aid."

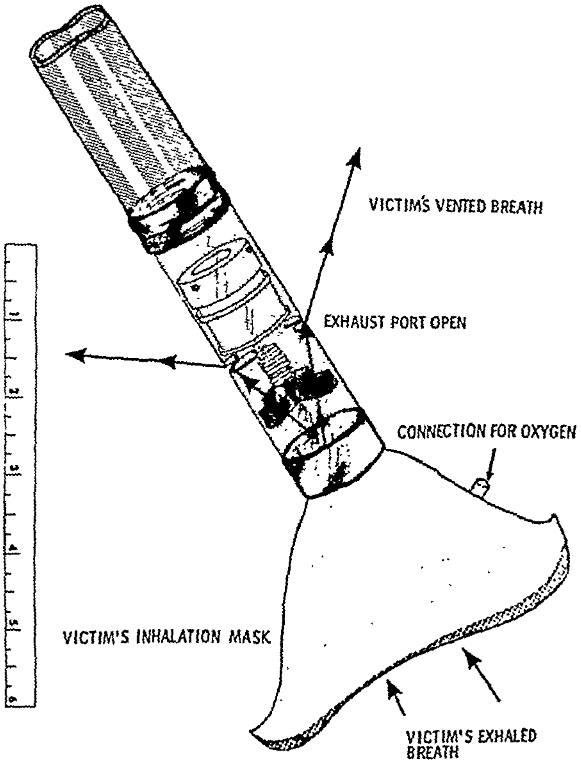

Fig. 2.—Passive phase of resuscitator unit.

The studies which were done by Gordon and associates,[1] Elam and associates,[2] and Greene and associates [3] have shown that expired-air ventilation is the only technique which assures an adequate tidal exchange in 100% of cases, as well as reasonable arterial oxygen and carbon dioxide levels. Our arterial carbon dioxide and oxygen studies agree with these studies and establish the efficacy of the Venti-Breather unit in expired-air artificial ventilation.

Airway pressures during mouth-to-mouth resuscitation[1] have been in a range of 0 mm. Hg during exhalation to 15 mm. Hg during inhalation, where the average tidal exchange was approximately 890 cc. Our results of pressure determinations using the Venti-Breather unit, as described under "Results," are somewhat lower. This is attributable to the fact that the catheter in our determinations was placed intratracheally, as opposed to intrapharyngeal placement.

In evaluation of this method, as well as the manual methods of artificial ventilation, it can be considered analogous to the "pressure-limited volume-variable" type of artificial ventilator described by Elam and co-workers.[4] It is time-cycled, in that the rate is fixed by the resuscitating individual. The volume delivered will vary according to the degree of "air flow obstruction" present. Air flow obstruction is an all-inclusive term used here to include upper airway obstruction by the tongue or mucus, lower airway obstruction by foreign bodies, or the degree of resistance imposed by the compliance factors of the lungs and chest cage. In certain individuals, the maintenance of a relatively unobstructed airway is difficult to accomplish by untrained individuals. Unless this can be accomplished, inadequate ventilation and gastric distention will result. In addition, a reasonably effective pressure seal must be maintained if an adequate tidal volume is to be delivered. The present techniques of expired-air resuscitation in adults require the resuscitator to use both hands to obtain an unobstructed upper airway and effective pressure seal, leaving no free hand to minimize gastric distention or perform other tasks. These present methods also require removal of resuscitator's mouth from that of the individual being resuscitated during exhalation.

This is obviated when this type of valve is used. The use of the valve with an attached oral airway and/or face mask greatly facilitates efforts of the resuscitator to establish a clear airway and maintain an effective airway seal, preventing pressure and volume losses. Evidence for this is that in the majority of subjects a patent airway and effective mask seal can be obtained with the use of one hand by an individual properly trained in the correct method of manual application and of holding a face mask. This training is simple and requires only a few minutes. As a result, the resuscitator in most instances will have a free hand with which to compress the stomach, minimizing any gastric distention which may occur. With further training, individuals can be taught to follow the pulse rate with the same hand which is holding the mask by palpating the facial artery with the fifth finger as it crosses the edge of the mandible.

Occasionally, an individual may be encountered in whom both hands are required to effect anterior displacement of the mandible before a patent upper airway can be established. The thumbs must then be applied to the mask to maintain an effective pressure seal. Rarely, a patent airway may only be established with the insertion of an oral airway. For these reasons training in these techniques should be given, but the necessity for such techniques will be the exception rather than the rule.

It is possible that this unit or a similar unit with a mask of suitable type and three sizes of oral airways could be standardized into an expired-air resuscitation "kit" for general use. The adoption of a kit compounds the amount of equipment and may cause doubt or hesitation lest one or more pieces should be lost or broken. However, individuals could be instructed to disregard the absence of a part or parts from the kit, including the Venti-Breather unit itself, by demonstration of the fact that every item of equipment merely facilitates the ease and increases the efficiency of the procedure. Thus, the absence of one or more items of equipment would not preclude the institution of expired-air ventilation.

Summary

The efficacy in expired-air ventilation of the Venti-Breather unit was evaluated by determinations of arterial carbon dioxide and oxygen content and airway pressures. The unit proved adequate in its durability and its ability to allow the achievement of adequate alveolar ventilation, as determined by blood carbon dioxide and oxygen studies.

The valve is considered a step in advancing public adoption of expired-air ventilation as a preferred means of resuscitative artificial ventilation.

Box 1559 (Dr. Lee).

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PURPURA FULMINANS TREATED SUCCESSFULLY WITH ANTICOAGULATION

REPORT OF A CASE

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The purpose of this report is to cite a case of purpura fulminans treated successfully with heparin sodium and to make a brief interpretive comment on the fundamental pathological process in this syndrome. The clinical and laboratory data suggested that thrombosis, not hemorrhage, is a primary mechanism of the pathological physiology.

The clinical syndrome variously known as purpura fulminans, purpura hemorrhagica, purpura gangrenosa, and purpura necrotica was first described by Guelliot in 1884 and later (1886) by Henoch. Since that time, more than 100 cases have been reported in which one of the above diagnoses has been made. The exact number is impossible to determine, because many clinical syndromes other than purpura fulminans are included in these reports. In retrospect, it is difficult to determine how many cases may represent meningococcemia, allergic purpura, idiopathic thrombocytopenic purpura, streptococcic and other types of bacteremia, or numerous other possible entities. The cases of purpura fulminans described recently have been characterized in more precise detail [1] and do seem to describe a single clinical entity.

Purpura fulminans is the catastrophic occurrence of massive areas of gangrene appearing abruptly during convalescence from a relatively benign infectious illness. Most of the cases have occurred in children. Onset usually occurs two to four weeks after scarlet fever. Less frequently, cases have been reported in the wake of chickenpox (varicella) [2] and streptococcic pharyngitis.[1d] The characteristic lesion is a large bluish-black patch of cutaneous gangrene. Often tissues beneath the skin are also involved. Rarely visceral involvement has occurred. The lesions usually occur on the extremities and are often strikingly symmetrical. They appear abruptly, progress rapidly, and are usually associated with signs and symptoms of severe systemic toxicity. Most of the reported cases were fatal within the first 48 to 72 hours. Those patients who survived longer displayed the evolutionary changes of massive gangrene, frequently necessitating amputation of extremities. Amputation has been the most frequently successful therapeutic measure. However, exchange transfusion, methionine, snake venom, vitamin K and rutin, and numerous other therapeutic measures are credited with some degree of success.

The pathological change is circumscribed epidermal and dermal necrosis with subcutaneous infiltration by red blood cells. Sometimes perivascular infiltration with inflammatory cells and intravascular coagulation have been demonstrable. Deficiencies of specific clotting factors in purpura fulminans include fibrinogenopenia, factor V deficiency, thrombocytopenia, and hypoprothrombinemia.

The etiology of purpura fulminans has not been established. The occurrence of this syndrome during convalescence from an infectious illness suggests that it may represent a hypersensitivity phenomenon. The similarity between the pathology of this lesion and that of the local Shwartzman phenomenon has been stressed.[1d]

A 14-year-old girl was admitted to the Barnes Hospital on Nov. 19, 1957. Her illness began four weeks prior to admission with the abrupt onset of fever, malaise, sore throat, cervical lymph node enlargement, and myalgia. Her parents thought she had a cold and she was treated with aspirin and bed rest. After some improvement, she had a mild exacerbation three weeks before admission, with fever and other symptoms but without sore throat, and was treated by her parents with a proprietary medicament containing aspirin, magnesium hydroxide, and yellow phenolphthalein. No other medicament was given. Nine days before admission, a painful bluish spot, "like a bruise," appeared on her right leg over the tibia and spread rapidly during the next few hours. She was seen by a physician and hospitalized. The following day a similar bruise-like patch appeared on the lower part of the left leg. That same day she was transferred to St. Joseph's Hospital in Hot Springs, Ark., as a patient of Dr. Driver Roland.

At that time the range of hematocrit values was 30-40%, the white blood cell counts varied from 13,000 to 26,000 per cubic millimeter, and the platelet count was 110,670 per cubic millimeter. The coagulation time (Lee-White) was greater than 45 minutes. Bleeding time was five minutes. The antistreptolysin-O titer was greater than 2,500 Todd units. Persistent and progressive fibrinogenopenia was suggested by the Fibrindex method,[3] in which a standard thrombin solution is added to the patient's plasma. The fibrin clot formation was consistently delayed and of poor quality. The prothrombin time was initially normal, but with fibrinogen depletion it became indeterminate because of lack of clot formation. Several grams of fibrinogen was given intravenously, and a quantitative fibrinogen determination shortly thereafter showed a value of 185 mg. per 100 ml.

Six days prior to her admission to Barnes Hospital, a third bluish patch developed on her left leg. Each lesion appeared in the skin and progressed rapidly in size during the first few hours, and then no subsequent enlargement was noted. In addition to intravenous injections of fibrinogen, the patient

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was treated with blood transfusions and adrenal steroids. On Nov. 19, 1957, the patient was flown to St. Louis and admitted to the Barnes Hospital.

There was no personal or family history of allergy or bleeding disorder. Physical examination revealed an acutely ill girl complaining bitterly of intense pain in both legs. Her face was flushed, and she avoided even the slightest motion of her legs. Vital signs included temperature, 38.6 C (101.6 F); blood pressure, 110/80 mm. Hg; pulse rate, 108 per minute; and respiration rate, 18 per minute.

Figure 1 shows the extent of the gangrenous extremity lesions, which were black with discrete outlines and a 1.5-cm. rim of erythema about each lesion. There were superficial bullae containing serosanguineous fluid in each lesion. Both legs were massively edematous, with signs of fluid in both knee joints. The left femoral, popliteal, posterior tibial, and dorsalis pedis pulses were not palpable. The left foot was cold and cyanotic, with poor capillary return. Position sense, however, remained intact in the left foot. Pulsations of the abdominal aorta were easily palpable.

Laboratory data were as follows: red blood cell count, 4,630,000 per cubic millimeter; white blood cell count, 17,300 per cubic millimeter; hemoglobin level,[4] 14.9 Gm. per 100 ml.; hematocrit value, 45%; and platelet count,[5] 130,000 per cubic millimeter. The silicone clotting time[6] was 20 minutes, three times as rapid as the normal values for this laboratory. The one-stage prothrombin time[7] was 18 seconds, with a control time of 22 seconds. The one-stage prothrombin time after barium sulfate–adsorbed plasma was added was 22 seconds, with a control time of 22 seconds. Fibrinogen level, determined gravimetrically, was 550 mg. per 100 ml., and fibrinolysin was not demonstrable. The antistreptolysin-O titer was greater than 500 units. The test for Rumpel-Leede phenomenon showed negative findings. Cultures of the fluid from a bulla on the left leg yielded a coagulase-negative white staphylococcus. A blood culture drawn on admission was sterile, and findings on urinalysis were completely within normal limits. Fecal specimens showed consistently negative results on guaiac testing. The serum bilirubin level, thymol turbidity, cephalin cholesterol flocculation, glutamic oxalacetic transaminase level, and albumin level were within normal limits.

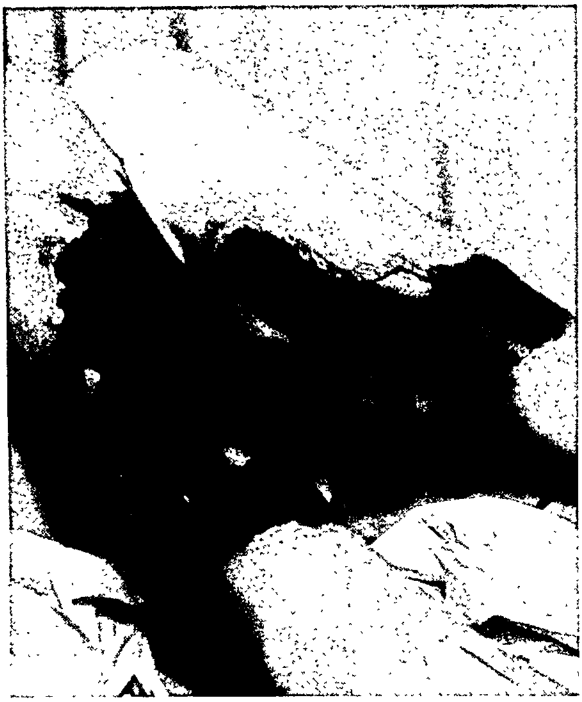

Fig. 1.—Appearance of lesions on patient's legs nine days after onset.

These data indicated accelerated coagulation with a normal fibrinogen level, slight factor V deficit, and mild thrombocytopenia. Because the clinical and laboratory evidence suggested a hypercoagulable state, with extensive superficial and deep thromboses, a continuous intravenous infusion of heparin was begun within a few hours after admission. It should be noted that anticoagulation was undertaken only after the patient's fibrinogen level was found to be adequate. She also received penicillin, streptomycin, methylprednisolone, and tolazoline hydrochloride.

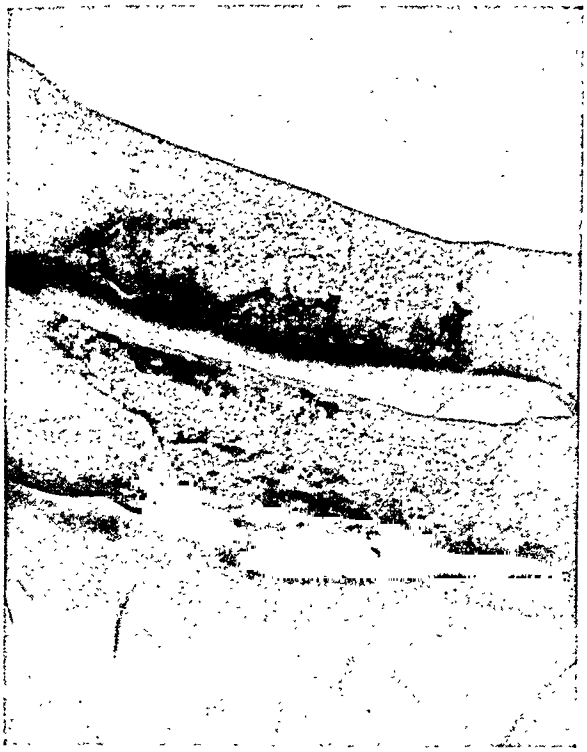

Fig. 2.—Appearance of skin grafts applied after surgical excision of eschars shown in figure 1.

During the first week of hospitalization, the patient had a low-grade fever and required narcotics for relief of pain in both legs. Gradual improvement was apparent, however. Her extremity lesions formed thick black eschars, her edema subsided, and the arterial pulses in the left leg became palpable. Her fibrinogen level never fell below 360 mg. per 100 ml. She showed neither evidence of bleeding nor the development of any new lesions.

On two consecutive days an anticoagulant dosage of warfarin (Coumadin) sodium was administered. On the 12th hospital day, the prothrombin time was 12% and the heparin infusion was discontinued. Although the prothrombin time remained less than 15%, within 12 hours the patient's right foot became edematous, cyanotic, painful, and pulseless. The diagnosis of deep venous thrombosis with reflex arterial spasm was made. Heparin therapy was reinstituted, with gradual subsidance of the process without any serious sequelae.

On the 15th hospital day the administration of heparin was temporarily discontinued and the patient was taken to the operating room for excision of the extremity lesions. At the time of surgery it was noted that the skin and subcutaneous tissue, and even muscle fascia in some areas, were necrotic. Excision was accomplished easily, and split thickness skin grafts were applied. Deep subcutaneous administration of heparin was done every six hours postoperatively and finally discontinued on the 34th hospital day. The patient's postoperative course was uncomplicated. Further grafting procedures were also successful. The patient required no amputation, although early in her hospital course this procedure was seriously considered. Figure 2 shows the appearance of the skin grafts in the early postoperative period.

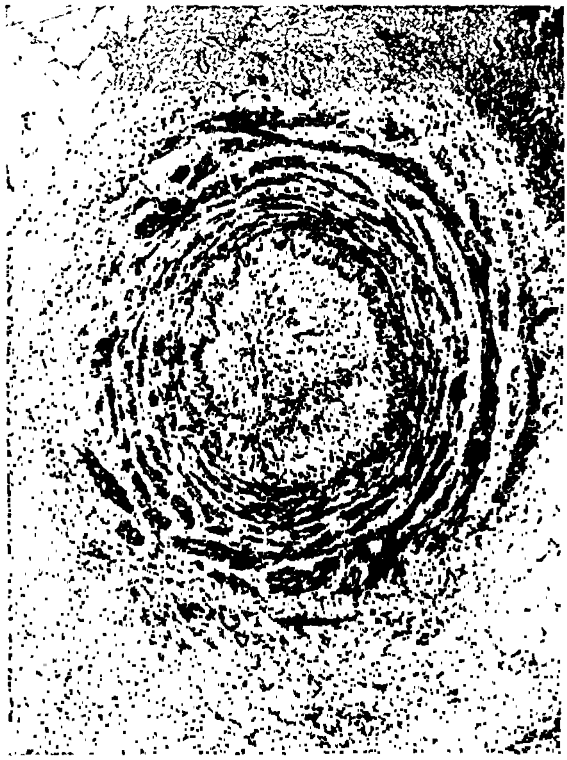

Fig. 3.—Subcutaneous vein occluded by organizing thrombus (Masson's trichrome stain, × 32).

The patient was discharged from the hospital 61 days after her admission. She was ambulant and essentially asymptomatic.

The microscopic pathology of the excised lesions is illustrated in figures 3, 4, 5, and 6. There was hemorrhagic necrosis of skin and underlying tissue with associated inflammatory reaction. Vascular changes were quite prominent. In necrotic regions, acute thrombophlebitis and secondary acute vasculitis were present. Thrombi were found in many medium-sized and small arteries and in both large and small veins. The thrombi were in all stages of organization. Although most of the thrombi were of the usual variety, a few were seen to be composed solely of fibrin.

Comment

The case described above is similar to those of purpura fulminans with fibrinogenopenia reported by Heal and Kent [1a] and Dyggve.[8] Koller and coworkers [1b] reported two cases associated with factor V deficiency. Other authors [9] have described patients with coagulation defects without specific identification of the factors involved. Earlier case reports called attention to variable degrees of thrombocytopenia.[10]

It is interesting to speculate about the mechanism of depletion of clotting factors in the present case and to consider the possibility of some common pathological mechanism which may cause depletion of fibrinogen, factor V, and platelets.

In any case of fibrinogen deficiency, there are three mechanisms which must be considered in its etiology: (1) diminished production of fibrinogen by the liver, (2) inactivation of fibrinogen by degradation of the molecule or by incorporation in an antigen-antibody complex, and (3) rapid peripheral utilization of fibrinogen to form fibrin, with or without the additional activation of fibrinolysis. In the patient described above, hepatic function tests revealed no evidence of liver disease. The possibility of degradation or inactivation of the fibrinogen molecule is more difficult to exclude, and there was no evidence to support or refute it. However, the postulated occurrence of extensive intravascular coagulation with resultant fibrin deposition was suggested by the appearance of the patient's legs. This impression was confirmed subsequently by the pathological findings. Data obtained from autopsy [1c] and surgical specimens [11] of other patients with purpura fulminans confirm the existence of extensive thrombosis in the region of the gangrenous lesions.

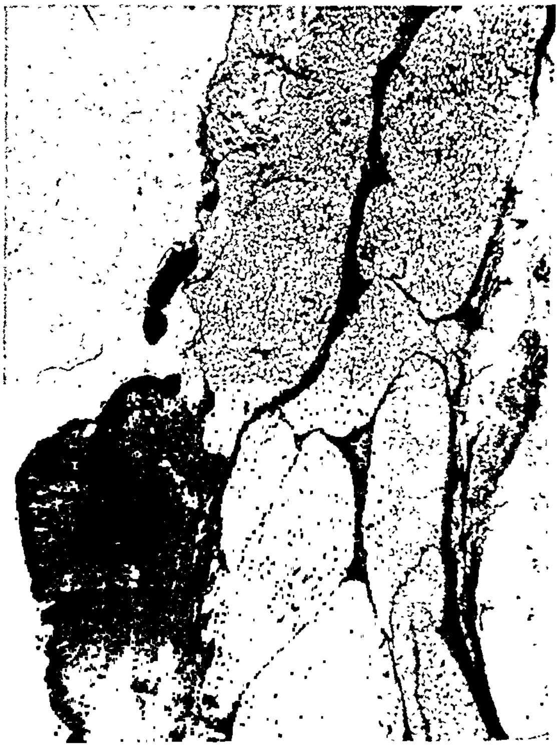

Fig. 4.—Skin margin with full thickness destruction and subcutaneous hemorrhagic necrosis (hematoxylin and eosin stain, × 8).

Schneider [12] and Ratnoff and Conley [13] have demonstrated that intravascular coagulation may result in fibrinogen depletion in man and in animals. Clinical syndromes in which intravascular defibrination is thought to exist are abruptio placenta, amniotic fluid embolism, retained dead fetus in utero, and, rarely, certain other obstetric complications. It is probably necessary to postulate an "infusion" of thromboplastic substances from the placental site in addition to coagulation in situ in order to explain the severe and rapid depletion of fibrinogen that occurs in these obstetric syndromes. However, Ashworth and Stouffer believe that rapid thrombosis within the placenta may account for complete depletion of available fibrinogen. It is impossible to say whether the release of tissue thromboplastin was a factor in the fibrinogenopenia demonstrated in this case. However, the widespread perivascular tissue damage and the presence of venous thrombosis far beyond the limits of the gangrene make this concept seem feasible.

It is interesting to note that a significant diminution of platelets and factor V has also been demonstrated in abruptio placentae associated with fibrinogenopenia. The relative severity of the depletion of fibrinogen, factor V, and platelets by coagulation would be determined by the nature and rapidity of the thrombotic process and the rate of their regeneration by the liver and bone marrow. The successful use of anticoagulation with heparin in purpura fulminans also lends support to the concept of intravascular defibrination with fibrinogen depletion in this syndrome.

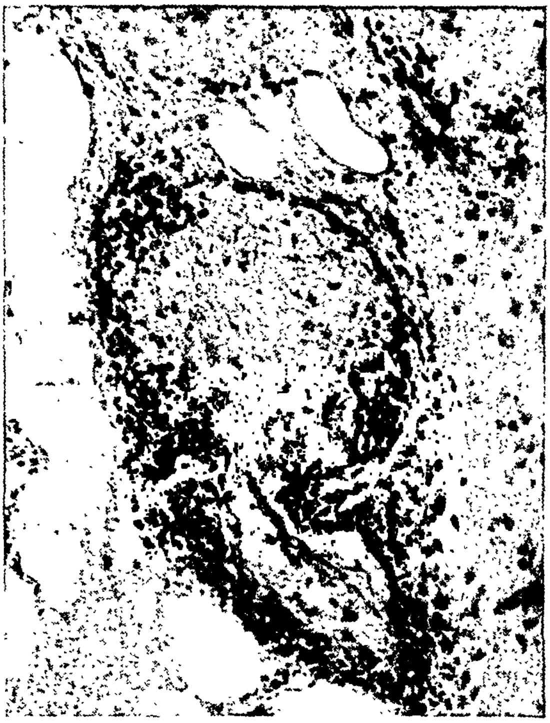

Fig. 5.—Perivascular inflammatory infiltration (hematoxylin and eosin stain, × 225).

The similarity between the Shwartzman phenomenon and purpura fulminans has become even more compelling since the interesting work of Stetson.[14] He described the histological characteristics of the local hemorrhagic necrosis of the Shwartzman phenomenon. The evidence strongly suggests that the capillary and venule occlusion that occurs is a primary mechanism and that, after interruption of the blood supply, necrosis of the involved vessels takes place and hemorrhage occurs later where the vessel walls have lost their integrity. Thomas and associates [15] have demonstrated a depletion of circulating fibrinogen after the second injection of challenge material (synthetic acid polymer) in the production of the generalized Shwartzman phenomenon. It is suggested that the intravascular deposition of fibrinoid and the subsequent necrotizing lesions characteristic of the generalized Shwartzman phenomenon may be due to the precipitation of fibrinogen. A qualitative change in the fibrinogen molecule, characterized by its increasing precipitability in vitro, was regularly demonstrable after the second injection of material used to elicit the Shwartzman phe-

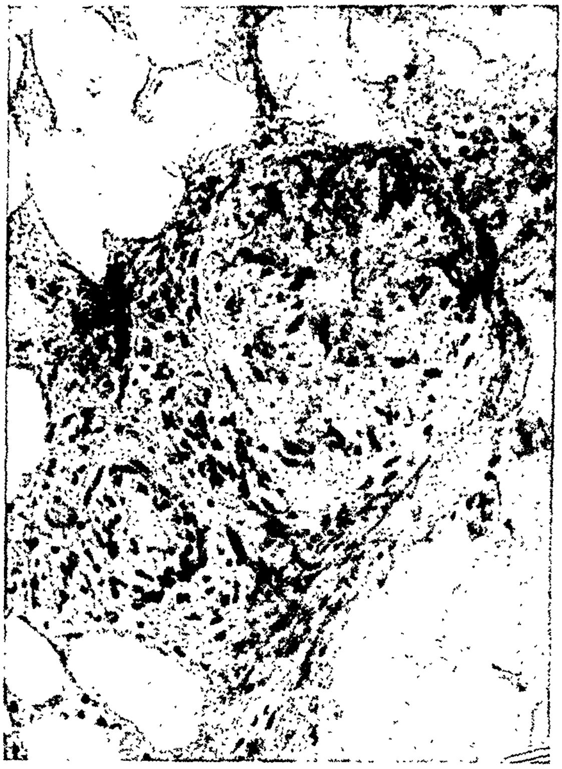

Fig. 6.—Small vessel with fibrin thrombus; larger vessel contains organizing thrombus (hematoxylin and eosin stain, × 210).

nomenon. These workers also demonstrated an inhibition of the Shwartzman phenomenon as well as fibrinogen depletion after pretreatment with heparin. If the lesions of purpura fulminans are analogous to those of the localized Shwartzman phenomenon, a second rationale for the therapeutic use of heparin is apparent.

In conclusion, it seems appropriate to suggest that the clinical and pathological entity designated as purpura fulminans is inappropriately categorized with the purpuras. Similar objection may be raised to other designations, i. e., purpura hemorrhagica and purpura gangrenosa, all of which somewhat inaccurately describe the pathological physiology of the characteristic lesion. Evidence is accumulating that the characteristic lesion in this syndrome is intravascular thrombosis and that hemorrhagic necrosis and depletion of coagulation factors are secondary phenomena. The somatic lesion of purpura fulminans is not typical purpura; this fact was noted in some of the earliest case descriptions. The lesion is a gangrenous one with extensive necrosis, and the extravasation of red blood cells probaby occurs only after vessel wall necrosis. Other authors[16] who previously described massive gangrene of extremities established that the lesion need not be confined to the skin and subcutaneous tissue. The dissatisfaction with the connotations of "purpura," in addition to the almost invariable association of the typical gangrenous lesion with a previous infectious illness, have prompted an effort to coin a more descriptive term. It is suggested that the descriptive phrase "postinfectious intravascular thrombosis with gangrene" be employed for the present time. Perhaps future studies of the basic pathological physiology and biochemistry of this disease will clarify its nature and thereby permit more exact nomenclature.

Summary

A case of purpura fulminans was treated successfully with heparin anticoagulation. The illness followed an episode of pharyngitis, presumably of streptococcic origin, and was associated with marked hypofibrinogenemia. Heparin was used as a therapeutic agent because clinical and laboratory data suggested extensive intravascular thrombosis and a hypercoagulable state. The proposal is made that purpura fulminans is basically a disease of thrombosis and gangrene. The pathological similarities between the lesions of purpura fulminans and those of the localized Shwartzman phenomenon support the hypothesis that purpura fulminans is fundamentally a thrombotic disease.

600 S. Kingshighway (10).

The patient's hospital care was supported by a fund established by the relatives of Dr. John Saxton, in his memory.

The heparin sodium used in this study was supplied as aqueous Heparin sodium and the methylprednisolone as Medrol by the Upjohn Company, Kalamazoo, Mich.; the tolazoline hydrochloride used in this study was supplied as Priscoline hydrochloride by Ciba Pharmaceutical Products, Inc., Summit, N. J.

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COUNCIL ON FOODS AND NUTRITION

VITAMIN PREPARATIONS AS DIETARY SUPPLEMENTS AND AS THERAPEUTIC AGENTS

The Council has authorized publication of the following statement.

Philip L. White, Sc.D., *Secretary.*

Vitamin preparations are used extensively and are valuable when used properly. For the most intelligent use and beneficial results in preventive or therapeutic medicine, the values and the limitations of vitamins should be realized. It is important that a clear differentiation be made between vitamins as dietary supplements and vitamins as therapeutic agents. The Council on Foods and Nutrition has reviewed the indications for administration of vitamins in supplemental and therapeutic amounts, the composition and dosage of vitamin preparations, and the possible dangers of excessive use of certain vitamins. The following is the Council's present position on this matter.

Recommended Dietary Allowances of Vitamins and Their Occurrence in Food

Vitamins are essential nutrients, and their usual source is food. All the nutrients essential to the maintenance of health in the normal individual are supplied by an adequate diet, one which fulfills the Recommended Dietary Allowances, revised 1958, developed by the Food and Nutrition Board, National Research Council (Publication 589). The levels of nutrients recommended are desirable goals in nutrition for all normal, healthy persons. They are believed to be adequate for maintaining good nutrition throughout life.

Normal Diets.—A convenient guide to the composition of an adequate diet has been prepared by the United States Department of Agriculture (Leaflet 424). Foods are classified according to their contribution of several nutrients, although emphasis is placed on key foods as important sources of certain nutrients. This daily food plan gives a basis for an adequate diet but permits the individual wide choice in his food selections. This is the fundamental plan:

Milk Group: Some milk daily—

Children	3 to 4 cups
Teen-agers	4 or more cups
Adults	2 or more cups
Pregnant women	4 or more cups
Nursing mothers	6 or more cups

Cheese and ice cream can replace part of the milk.

Meat Group: Two or more servings, including—Beef, veal, pork, lamb, poultry, fish, eggs, with dry beans and peas and nuts as alternates.

Vegetable-Fruit Group: Four or more servings, including—A dark green or deep yellow vegetable important for vitamin A—at least every other day. A citrus fruit or other fruit or vegetable important for vitamin C—daily. Other fruits and vegetables including potatoes.

Bread-Cereals Group: Four or more servings—Whole grain, enriched, restored.

This fundamental plan will supply the adult with one-half to two-thirds of the caloric allowance, four-fifths of the iron, four-fifths of the thiamine, nine-tenths of the niacin, and all of the riboflavin allowances. These nutrients and others not mentioned will be raised to adequate amounts by the other foods normally included in the daily diet but not specifically mentioned in the basic plan. Foods such as butter, margarine, other fats and oils, sugars, desserts, jellies, and unenriched grain products serve to fulfill the caloric and nutrient allowances.

Table 1.—*Minimum Daily Requirements Compared with Recommended Dietary Allowances*

Vitamin*	M.D.R., Adults	R.D.A., Man, Aged 25	M.D.R., Children, 6-11 Yr.	R.D.A., Children, 7-12 Yr.
Vitamin A, U.S.P. units	4,000	5,000	3,000	3,500-4,500
Thiamine, mg.	1.0	1.6	0.75	1.1-1.3
Riboflavin, mg.	1.2	1.8	0.9	1.5-1.8
Vitamin C, mg.	30	75	20	60-75
Vitamin D, U.S.P. units	400	...	400	400

* Comparable figures for niacin are not given since the Recommended Dietary Allowances include preformed niacin and niacin made available from tryptophan, whereas the Minimum Daily Requirements consider only preformed niacin.

Therefore, if the diet contains the key food groups in sufficient amounts, nutritional supplementation should be unnecessary. The proper selection and preparation of foods are important to the achievement of an adequate diet.

Minimum Daily Requirements.—The Recommended Dietary Allowances should not be confused with the Minimum Daily Requirements established for labeling purposes by the Food and Drug Administration. Nutrient contents can thus be expressed in terms of the proportion of daily requirements supplied. Minimum Daily Requirements are the amounts of nutrients needed to prevent symptoms of deficiency and to provide a small factor of safety. Recommended Dietary Allowances are amounts of nutrients which will maintain good nutrition in essentially all healthy persons. Table 1 demonstrates the basic differences between the two concepts. Throughout this statement the Recommended Dietary Allowances will be used.

Vitamins as Dietary Supplements

Healthy persons whose diets are ordinarily considered adequate may benefit from supplementary vitamins at certain special periods of life, such as during pregnancy and lactation. Vitamin supplementation is useful during periods of illness or deranged mode of life, which may result in impairment of absorption of nutrients or deterioration of dietary quality. Supplementation may also be of value to the individual who, through ignorance, poor eating habits, or emotional or physical illness, does not eat an adequate diet. The physician's primary responsibility for these patients is to remove these disturbing factors rather than merely to alleviate their results. Nevertheless, until the disturbing factors have been discovered and, when possible, removed, supplementary vitamins are valuable in assuring adequate intake.

Infants and Children.—The daily diet of the artificially fed infant should be supplemented with vitamins C and D if the diet does not supply 30 mg. of vitamin C and 400 U. S. P. units of vitamin D. The diet should be brought up to these amounts, with care exercised that the intake of vitamin D is not excessive. The requirement of the breast-fed baby for vitamin D is not accurately known, but it is accepted practice to advocate 400 U. S. P. units of vitamin D supplement daily. Administration of vitamin D and, in artificially fed babies, of vitamin C should be started with the introduction of artificial feeding. Too often administration of vitamin C is delayed even into the second month. When administration of the vitamins is started, the amount of vitamin D is often too great and the amount of vitamin C too small. Maximum calcium and phosphorus retentions are obtained with 300 to 400 U. S. P. units of vitamin D daily. Not only are retentions no greater with larger amounts, but the use of 1,800 U. S. P. units or more daily for several months decreases appetite and, as a consequence, reduces the total retentions of calcium and phosphorus and slows linear growth. Infants receiving unfortified skimmed milk formulas also require supplements of vitamin A (1,500 U. S. P. units daily).

Healthy children fed adequate amounts of wholesome foods need no supplemental vitamins except vitamin D, which should be supplied throughout the growth period. An adequate intake of vitamin D-fortified homogenized milk or reconstituted evaporated milk (1½ to 2 pt. daily) provides the vitamin D required. The physician should determine the approximate amount of vitamin D supplied by foods before supplementing the diets. In certain instances, physicians may wish to supplement the diets of infants and children with preparations containing vitamins A, C, D, and certain B vitamins. The Council believes that such preparations containing the B complex are not needed for routine use but would be of value for children with special problems. It is important that the growing child be introduced to a wide variety of wholesome foods, since food is the normal source of nutrients.

Adults.—Healthy adults receiving adequate diets have no need for supplementary vitamins except during pregnancy and lactation when 400 U. S. P. units of vitamin D daily are required if the intake of vitamin D-fortified milk is low. In these periods of physiological stress, if any doubt exists as to the adequacy of the previous or present diet, supplementary vitamins in addition to vitamin D should be administered.

Supplementary vitamins are useful during periods of emotional illness, which result in bizarre food habits or greatly diminished food intake. The choice of vitamin preparations to be used to insure a desirable nutrient intake in such instances should be based upon the physician's evaluation of the patient's dietary pattern.

When restricted or nutritionally inadequate diets are prescribed for pathological conditions, vitamin mixtures as supportive supplements are indicated. Examples of conditions in which such diets may be instituted include allergic states and chronic diseases of the gastrointestinal tract. Vitamin supplementation also is indicated when it is necessary to employ parenteral feeding. The character of the supplementation required will depend on the diet, the nutrients administered, and the period of time the regimen is maintained.

In any prolonged illness associated with decreased food intake or in other situations in which an individual is unable or unwilling to eat an adequate diet, the physician must decide whether supplementation is necessary. The extent of the illness or the nature of the dietary restriction should be evaluated to determine whether the level of vitamin supplementation should be equal to allowances under normal physiological conditions or in excess of them.

Nutrition surveys in several areas of the United States have indicated that a variable fraction of certain segments of the population is not receiving sufficient varieties of foods to supply vitamins in amounts necessary to meet the Recommended Dietary Allowances. Generalization of these findings as a basis for vitamin supplementation of healthy individuals is not rational. The methodology employed in these surveys and the standards used for interpretation have varied considerably. It is necessary for the physician to evaluate each person individually. Correction of inadequacies should then be instituted, preferably by a proper diet, although supplementation with vitamins may be necessary until dietary adjustments are made and the body stores repleted. Avoidance of excessive or unnecessary supplementation is, of course, desirable.

Multivitamin Combinations

Multiple vitamin preparations should contain only those vitamins shown to be essential in human nutrition or metabolism. The Council recognizes that certain foods such as liver, yeast, and wheat germ are excellent sources of some of the vitamins but finds no evidence to justify special claims for such materials or their concentrates in multivitamin mixtures. The combination of vitamins in a supplementary mixture should have a rational basis. Several combinations meet these criteria.

1. A combination of all the vitamins that have been demonstrated to be essential in human metabolism may be desirable for supplementation of certain restricted diets. Such preparations would include vitamins A and D, ascorbic acid, thiamine, riboflavin, niacin, pyridoxine, pantothenic acid, folic acid, and vitamin B_{12}. Vitamin K is not included, because dietary deficiency rarely occurs and because this vitamin has special uses which are not adapted to inclusion in multiple vitamin preparations, for example, prophylactic use for pregnant women and newborn infants. Vitamin D would be included in preparations for children, adolescents, and pregnant or nursing women and would be optional in others.

TABLE 2.—*Recommended Daily Dietary Allowances, Revised 1958*[*]

	Age, Yr.	Weight, Kg. (Lb.)	Height, Cm. (In.)	Calories	Protein, Gm.	Calcium, Gm.	Iron, Mg.	Vitamin A, U.S.P. Units (I.U.)	Thiamine, Mg.	Riboflavin, Mg.	Niacin,[†] Mg. Equiv.	Ascorbic Acid, Mg.	Vitamin D, U.S.P. Units (I.U.)
Men	25	70 (154)	175 (69)	3,200[‡]	70	0.8	10	5,000	1.6	1.8	21	75	...
	45	70 (154)	175 (69)	3,000	70	0.8	10	5,000	1.5	1.8	20	75	...
	65	70 (154)	175 (69)	2,550	70	0.8	10	5,000	1.3	1.8	18	75	...
Women	25	58 (128)	163 (64)	2,300	58	0.8	12	5,000	1.2	1.5	17	70	...
	45	58 (128)	163 (64)	2,200	58	0.8	12	5,000	1.1	1.5	17	70	...
	65	58 (128)	163 (64)	1,800	58	0.8	12	5,000	1.0	1.5	17	70	...
Pregnant (second half)				+300	+20	1.5	15	6,000	1.3	2.0	+3	100	400
Lactating (850 ml. daily)				+1,000	+40	2.0	15	8,000	1.7	2.5	+2	150	400
Infants[§]	0-1/12[§]	...	...	...	...	...	...	...	...	...	...	...	...
	2/12-6/12	6 (13)	60 (24)	kg.x120	...	0.6	5	1,500	0.4	0.5	6	30	400
	7/12-12/12	9 (20)	70 (28)	kg.x100	...	0.8	7	1,500	0.5	0.8	7	30	400
Children	1-3	12 (27)	87 (34)	1,300	40	1.0	7	2,000	0.7	1.0	8	35	400
	4-6	18 (40)	109 (43)	1,700	50	1.0	8	2,500	0.9	1.3	11	50	400
	7-9	27 (60)	129 (51)	2,100	60	1.0	10	3,500	1.1	1.5	14	60	400
	10-12	36 (79)	144 (57)	2,500	70	1.2	12	4,500	1.3	1.8	17	75	400
Boys	13-15	49 (108)	163 (64)	3,100	85	1.4	15	5,000	1.6	2.1	21	90	400
	16-19	63 (139)	175 (69)	3,600	100	1.4	15	5,000	1.8	2.5	25	100	400
Girls	13-15	49 (108)	160 (63)	2,600	80	1.3	15	5,000	1.3	2.0	17	80	400
	16-19	54 (120)	162 (64)	2,400	75	1.3	15	5,000	1.2	1.9	16	80	400

[*] From Food and Nutrition Board, National Research Council. Allowance levels are designed for maintenance of good nutrition for normal, healthy persons living under usual environmental stresses in a temperate climate in the United States. Recommended allowances can be attained with a variety of common foods, providing other nutrients for which human requirements have been less well defined. See text of Recommended Dietary Allowances, published by National Research Council, for more detailed discussion of allowances and of nutrients not tabulated.

[†] Includes dietary sources of preformed vitamin and precursor, tryptophan; 60 mg. of tryptophan = 1 mg. of niacin.

[‡] Applies to individuals usually engaged in moderate physical activity. For office workers or others in sedentary occupations they are excessive. Adjustments must be made for variations in body size, age, physical activity, and environmental temperature.

[§] The Board recognizes that human milk is the natural food for infants and feels that breast feeding is the best and desired procedure for meeting nutrient requirements in the first months of life. No allowances are stated for the first month of life. Breast feeding is particularly indicated during the first month when infants show handicaps in homeostasis due to different rates of maturation of digestive, excretory, and endocrine functions. Recommendations as listed pertain to nutrient intake as afforded by cow's milk formulas and supplementary foods given the infant when breast feeding is terminated. Allowances are not given for protein during infancy.

2. A combination of vitamins having complementary metabolic functions should prove useful in supplementation of certain restricted diets. These preparations might include (*a*) a combination of the B vitamins, thiamine, riboflavin, and niacin, with or without pyridoxine, pantothenic acid, folic acid, or vitamin B_{12}; (*b*) the B vitamins listed under (*a*) in combination with ascorbic acid; or (*c*) a combination of a calcium salt and vitamin D in a stable form.

3. A combination of vitamins that might be expected to be lacking concomitantly because of their common distribution in foods also might be desirable for supplementation. Examples would include the fat-soluble vitamins A and D or vitamins of the B complex as previously noted.

Quantities for Dietary Supplementation.—The quantities of vitamins included in mixtures for dietary supplementation should furnish daily an amount which approximately fulfills, but does not greatly exceed, the Recommended Dietary Allowances for vitamins as given in table 2. The physician should exercise more caution that his recommendations are not increased in amount and that his patients do not follow the precept that greater concentrations of vitamins are justified, in light of the little additional cost. There is a tendency for the patient to believe that, if a little is good, more would be better. It has not been demonstrated that larger amounts are beneficial under ordinary physiological conditions; in fact, an overdosage of vitamins A or D can be harmful.

The multivitamin preparations available today fall into three general categories, those that supply (1) about one-half the Recommended Dietary Allowances, (2) one to one and one-half times the Recommended Dietary Allowances, and (3) three to five times the Recommended Dietary Allowances. The Council considers the first class of preparations useful in dietary supplementation in situations as noted in the section entitled Vitamins as Dietary Supplements. The preparations containing one to one and one-half times the Recommended Dietary Allowances (group 2) would be useful when supplementing therapeutic diets or when prolonged illness or other causes significantly reduce food intake. After the normal diet is instituted, these higher potency preparations are not needed. The third general type of preparations containing three to five times the Recommended Dietary Allowances should be reserved for use in therapy as discussed in the section on Vitamins as Therapeutic Agents.

Recommended Dietary Allowances have not been established for pyridoxine, pantothenic acid, folic acid, or vitamin B_{12}, although all these substances are essential in human metabolism. The amounts present in diets considered adequate in other factors should serve as a guide for quantities to be used in supplementation. The amount of folic acid in supplementary vitamin mixtures should be no greater than that available from an abundant dietary. Common experience indicates that this is a quantity which will seldom support hematological function in pernicious anemia and therefore will not mask the diagnosis of this disorder. Although this quantity is still to be determined, 0.3 mg. of folic acid is suggested tentatively as a proper maximum amount for supplemental mixtures.

An abundant dietary provides 2 to 10 mcg. of vitamin B_{12}, 5 to 10 mg. of pantothenic acid, and 1 to 3 mg. of pyridoxine. Therefore, these levels are considered satisfactory in vitamin mixtures for dietary supplementation. Supplementary vitamins administered in the amounts suggested are safe. If the amount of one or more of the vitamins in these mixtures is markedly less than the recommended allowance, the supplemental value of the preparation may be limited accordingly.

Combination of Vitamins and Minerals.—Minerals have been combined with vitamins in mixtures for dietary supplementation. Although certain supplemental vitamin mixtures with calcium, iron, or with both minerals have proved useful, there is no good evidence to support the inclusion of the 12 or more mineral elements essential for man. Few of these minerals are likely to be lacking, even in restricted diets. When iron is needed as a dietary supplement, it should be given as such in most instances. Iron and calcium might be included as optional ingredients in certain supplemental vitamin mixtures, for example, for administration during pregnancy. A combination of calcium and vitamin D in stabilized form may be useful. Sodium, chlorine, and iodine are usually supplied by iodized table salt. Supplementation with copper is rarely needed since it is usually adequately supplied by the diet. Evidence is lacking that addition of the trace elements, such as manganese, zinc, cobalt, and molybdenum, to the human diet is needed.

Vitamins as Therapeutic Agents

Vitamins in therapeutic amounts have proved valuable in both specific therapy and in supportive therapy in numerous pathological states. Vitamins in therapeutic amounts are indicated only in the treatment of deficiency states or pathological conditions in which requirements are increased.

Therapeutic vitamin mixtures should be so labeled and should not be used as dietary supplements. The decision to employ vitamin preparations in therapeutic amounts clearly rests with the physician, and the importance of medical supervision when such amounts are administered is emphasized.

The quantities of vitamins included in mixtures intended for therapeutic use in the treatment of multiple vitamin deficiencies should approximate simple multiples of the amounts recommended in the National Research Council's Recommended Dietary Allowances, revised 1958. It is seldom necessary to administer vitamins in amounts greater than three to five times the Recommended Dietary Allowances. In the rare instances in which larger quantities seem indicated, the vitamin(s) in question should be given separately. Although there is little danger of harm from larger quantities of the water-soluble vitamins because the excess is excreted readily, there is real danger of toxicity from larger amounts of fat-soluble vitamins because the excess accumulates in the body. In multivitamin preparations, the amount of vitamin D should not exceed three times the Recommended Dietary Allowances as previously stated.

The combination of vitamins in mixtures intended for therapy should have a rational basis. Suitable combinations include (1) vitamins that have complementary metabolic functions and (2) vitamins that might be expected to be lacking concomitantly according to their common distribution in foods, or to similar chemical properties which influence absorption and biological availability. Examples would include (1) a combination of the B vitamins, thiamine, riboflavin, and niacin, with or without pyridoxine and calcium pantothenate; (2) a combination of these B vitamins with ascorbic acid; and (3) a combination of fat-soluble vitamins A and D or A, D, and K. In addition, a combination of vitamins A, D, ascorbic acid, thiamine, riboflavin, and niacin, with or without pyridoxine or calcium pantothenate, may be desirable.

There is little evidence which warrants inclusion of folic acid and vitamin B_{12} in therapeutic amounts in vitamin mixtures. As noted previously, folic acid in therapeutic dosage may mask the diagnosis of pernicious anemia and permit neurological lesions to develop while maintaining hematological remission. When folic acid is indicated in therapeutic quantities, it should be administered separately. The need for inclusion of vitamin B_{12} in therapeutic vitamin mixtures in an amount in excess of that supplied by an abundant dietary has not been demonstrated to date.

Before vitamins or other therapeutic agents are prescribed in the treatment of anemia, the etiology of the anemia should be determined. This will permit administration of the proper hematinic agent, which will usually be a single factor, namely, vitamin B_{12}, folic acid, or iron. Preparations containing all or most of the known antianemic factors, vitamin B_{12}, intrinsic factor, folic acid, iron, ascorbic acid, and copper, are, in the opinion of the Council, not justifiable.

Toxicity of Vitamins A and D

Inclusion of excessive amounts of fat-soluble vitamins in therapeutic mixtures is scientifically unwarranted and potentially dangerous. The absence of excretory pathways for vitamins A and D and for carotene makes it necessary to limit their intake in order to avoid the development of hypervitaminosis. Daily dosage of more than 25,000 U. S. P. units of vitamin A should be followed carefully for toxicity.

Hypervitaminosis A.—Apparently the body can tolerate quantites of vitamin A 100 times greater than the daily physiological requirement, but there is a definite possibility of harm from the prolonged ingestion of vitamin A in excess of 50,000 U. S. P. units daily. Chronic vitamin A intoxication occurs more frequently in children than in adults. Depending upon the severity of the intoxication, children older than one year may develop anorexia, weight loss, irritability, fretfulness, pruritus, seborrhea-like cutaneous eruptions, fissuring at the corners of the mouth, and cracking and bleeding of the lips. Later signs include hepatomegaly, hydrocephaly, alopecia, painful swellings over the long bones with bone and joint pains and bone tenderness, hyperostosis, deep, hard, tender swellings in the extremities, and cortical thickening in tubular bones. Serum vitamin A levels are increased and are useful diagnostically. Vitamin A intoxication in adults causes symptoms which are similar to those of hypervitaminosis A in children but are usually milder. Structural bone changes are not likely to occur, and bone and joint pains are not so severe. Menstrual alterations, exophthalmos, and pigmentation of the skin have been reported. Transitory increased intracranial pressure has been noted in severe acute toxicity.

Hypervitaminosis D.—There is great variation in individual tolerance to large amounts of vitamin D. Several factors influence response to continued ingestion of large amounts of vitamin D, including exposure to ultraviolet light, dietary calcium, and the endocrine system. A daily intake of 1,800 U. S. P. units continued over long periods of time may be mildly toxic in children. However, in the uncommon syndrome, refractory rickets, as much as 50,000 to over 100,000 U. S. P. units daily may be tolerated or, indeed, required.

The early symptoms of vitamin D intoxication include anorexia, nausea, headache, polyuria and nocturia, and diarrhea. Pallor and lassitude are also common findings in children. Later symptoms and signs include weakness, fatigue, renal damage, metastatic calcification, and depression. Hypochromic, normocytic anemia with azotemia has been reported in adults with hypervitaminosis D. When large dosages of vitamin D are administered, frequent determinations of serum and urine calcium should be made. An increase in the serum calcium to a level above 11 mg. per 100 ml., occurring in association with a high intake of vitamin D, is an indication for interdiction of the vitamin D supplement.

Comment

Vitamin mixtures, other than those discussed herein, may be demonstrated to be useful in therapy by further research. Until adequate scientific evidence is presented as to their value, however, such mixtures should not be advocated for general use. Public health will be served best by insistence on a factual basis for vitamin supplementation and therapy. It is sound judgment to emphasize repeatedly that properly selected diets are the primary basis for good nutrition.

FRONTIERS AND NEW VISTAS.—The frontiers and new vistas urgently awaiting attention are not in physical and chemical research and engineering but in man himself; not in technologies but in the wisdoms that give meaning and direction to them. Science has released to us tremendous energies and opportunities, but we must turn inward for understanding and direction of these things. As scientists our opportunity is to see the interdependence of our individual specialties and the order of the Universe, of our individual selves and all mankind. We must understand more about healthy self-interest and our interdependence for we have neglected their importance to the lopsided cultivation of profits, power, prestige and "success," pseudovalues, mirages and means rather than ends. We are part of humanity, units of living and loving and reasoning that are genuine communities, whose members are part of each other not in standardized parts but in common eagerness for the same values.—J. A. Aita, M.D., and G. A. Young, M.D., Love, Affection and Human Relatedness, *The Nebraska State Medical Journal,* September, 1958.

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FORT RITCHIE CONFERENCE ON YOUTH FITNESS

THE third nationwide conference on the fitness of American youth was held at Fort Ritchie, Md., Sept. 9 and 10, 1958. The first such conference was held at the U. S. Naval Academy, Annapolis, Md., in June, 1956, having been postponed from September, 1955, owing to the illness of President Eisenhower. The second conference was held at the U. S. Military Academy, West Point, N. Y., in September, 1957. The first meeting was in the nature of an *ad hoc* conference out of which sprang two recommendations, namely, the establishment of a President's Council on Youth Fitness at Cabinet level and an advisory committee of outstanding citizens to work with and advise the Council. The President acceded to the recommendations of the *ad hoc* conference, creating the Council and the Advisory Committee. The meetings at West Point and Fort Ritchie, therefore, represent the first and second meetings of the Council with the Advisory Committee.

The Council now consists of the Secretary of the Interior (Chairman) plus the Secretary of Defense; the Secretary of Agriculture; the Secretary of Labor; the Secretary of Health, Education, and Welfare; the Secretary of Commerce; and the administrator of the Housing and Home Finance Administration. The two latter were added to the membership of the Council at the Fort Ritchie meeting. The chairman of the Citizens' Advisory Committee is Homer C. Wadsworth, executive director, Kansas City Association of Trusts and Foundations. Five practicing physicians are included in the 100 citizens on the Advisory Committee, plus two public health physicians and two dentists.

The Fort Ritchie meeting marked the completion of two years of activity since the Annapolis meeting following which Shane McCarthy, J.D., was appointed executive director of the President's Council and established with a small staff in Washington, D. C. The activities of the Council have been largely promotional in nature. The director spends an enormous amount of time and energy and covers great distances in going to all parts of the United States to engender enthusiasm for the improvements needed in the fitness of American youth.

Among the basic principles enunciated from the beginning and reaffirmed at the Fort Ritchie meeting was the avoidance of any new and over-all agency of government to carry out the work. In the words of Mr. Wadsworth summarizing the proceedings of the Fort Ritchie conference, "There is a singular agreement in your reports, that you are as unprepared as the President originally was—and the Council currently is—to see grow up any vast new bureaucracy in government. In fact, you have brought forth many constructive suggestions on how the existing instrumentalities of government at all levels may more appropriately serve the interest of youth than is currently the practice, and this is part of our obligation. In effect, you have reaffirmed the American way of dealing with social, educational, and cultural problems, and it is heartening that this is so."

In an able summary of the proceedings, Chairman Wadsworth pointed out five major objectives of the program of the Council, in which the Advisory Committee concurred: First, there was emphasis on correct information, appraisal, and research; second, it was recommended that an informational kit be developed for the guidance of communities who may be seeking to initiate their own programs promoting youth fitness; third, it was recommended that the purposes and the program of the Council be more effectively publicized and promoted for the information of the American people and in order to enlist their support; fourth, the Council is visualized as a clearing house and a catalyst, and not an operating agency; fifth, the Council staff is to make every effort to draw on the experience of those who have been working in youth-serving agencies in order that newcomers in the field may be adequately oriented and prepared, and there may be a minimum of lost motion, needless experimentation, and amateur bungling.

The Citizens Advisory Committee rather boldly challenged the members of the President's Council with the fact that few of them had attended previous meetings with the Advisory Committee and, those who had, did not stay through the meeting. They invited the members of the President's Council to be present throughout the meeting and to participate in the working groups. Actually, the attendance from Cabinet members at the Fort Ritchie meeting was about as good as could be expected from men with the responsibilities of Cabinet officers. Chairman Seaton stayed throughout the entire meeting; Secretary Benson was present in person during part of the meeting; the Secretaries of Defense and of Health, Education, and Welfare, and the Secretary of Labor, were represented by Undersecretaries. The two newly added departments also were represented by high-ranking staff officials.

For the first time at this meeting there were organized in addition to the eight working groups of diversified character, the so-called special interest groups, one of which represented the health interests—the medical and dental professions, the public health, and other allied groups. These special interest groups made useful contributions to the final deliberations.

Among general recommendations contained in the report that should be of interest to physicians may be mentioned the following: (1) that National Youth Fitness Week be proclaimed in time to permit sufficient advance planning and action by all organizations and avoid conflicts with other national weeks; (2) that after the Youth Fitness Week, local committees evaluate their remaining needs for an effective fitness program and integrate these with facilities available from local authorities; presumably, physicians in many local areas are now serving in active or advisory positions as part of their contribution to the general fitness program; (3) that the Council develop promotional materials by which communities can appraise all current plans, actions, and services relating to youth fitness, and ascertain gaps, inadequacies and inequalities in local plans and actions indicating barriers and deterrents to effective accomplishment of youth fitness goals, and the Council prepare and distribute an information kit for community action, so communities can help themselves in starting and carrying on effective youth fitness action programs in the broadest concept of the term. This kit should include suggested guides for inventorying community facilities, as well as leadership and organizational resources. It should also include suggestions on how the community can organize an appropriate local group designed to secure more, coordinated action by public and private community agencies, including the local school system.

Additionally, it was recommended that community councils and national organizations be encouraged to appoint fitness liaison offices whose function will be to report significant accomplishments and successful techniques to the Council staff and that the Council staff be asked to compile and disseminate accomplishments in the form of a periodic community action newsletter.

It was suggested that the Executive Committee of the President's Citizens Advisory Committee of the Council issue a quarterly newletter stating specifically the progress that has been reported among the States or among the agencies of government in furthering youth fitness programs. It was emphasized that members of the Advisory Committee should stand ready, when requested by the President's Council, to carry the youth fitness message to the states and local communities through speeches and attendance at meetings.

Among future activities resulting from the Council meeting may be a meeting of the leaders of existing National Youth Organizations to focus attention on their programs and secure their cooperation. Also, it will be suggested that the President write to those governors who have not, at yet, formed a Youth Fitness Committee, urging them to do so, and suggesting that the President's Advisory Committee members in each state lend assistance in forming such a committee. It also was recommended that the Council seek to have the youth fitness program placed on the agenda of the Annual Conference of Governors.

A copy of the report on the Fort Ritchie meeting, prepared by Mr. Seaton, can be obtained from the Superintendent of Documents, U. S. Government Printing Office, Washington 25. The price is 25 cents. Full title is "A Report to the President of the United States on the 1958 Fort Ritchie Meeting of the Council on Youth Fitness with the Citizens' Advisory Committee."

The medical representatives at the conference agreed that there was nothing in the proceedings to which the medical profession would be likely to take serious objection. As to supporting the President's program, the time-honored interest of the medical profession in the health of our people at any age is all the pledge that is needed to assure the President and his Council and the Citizens' Advisory Committee that the medical profession will not be lacking when opportunity arises for constructive action.

NUMBERING THE PAGES IN THE JOURNAL

A recent regulation of the U. S. Postoffice Department requires that periodicals mailed at second class postage rates number their pages in each issue in sequence. Accordingly, beginning with this issue, The Journal will use a dual pagination system. The page numbers of the editorial pages will continue to appear in boldface type and the issue page numbers will be placed in front of them in lightface type. An example of this is 50/2. This means the 50th page of the issue and the second editorial page. On the next page the pagination would be 51/3, and so on. This dual numbering system will enable The Journal to maintain continuity in the pagination of editorial content from issue to issue, and, at the same time, it will comply with the new postal regulation.

ORGANIZATION SECTION

STATEMENT ON JOINT CONFERENCE COMMITTEE

Preamble

As the art and science of medicine have become more complex and more comprehensive, hospital services, of necessity, have followed suit in an effort to produce maximum results from medical progress. For this reason and because of the other joint and separate responsibilities which physicians and hospitals have in providing medical care and hospital services, organization and cooperation are essential.

These responsibilities cannot be discharged with maximum effectiveness without proper liaison between doctor and hospital, the doctor being represented in an organized manner by a medical staff and the hospital by its governing body and that body's designated representative, the administrator.

In addition to, but not in conflict with, regular established lines of authority and responsibility, there should be a common ground where these two groups can meet in order that there may be a mutual understanding of each other's activities and problems, A suitable medium for this interchange of information and discussion is the Joint Conference Committee.

This document seeks to encourage the development and to strengthen the role of the Joint Conference Committee of the Board of Trustees and medical staff. It urges the establishment of such Joint Conference Committees because it believes that they will bring to bear on major decisions which must be made in the hospital a full measure of broad experience, intelligence, and responsibility.

Such a committee should be a part of the organizational structure of every hospital. It should exist even where there is medical staff representation on the governing board. The representatives of this committee meet, not as representatives of the departments from which they were chosen but as members of the committee as a whole, in the interest of the patient, the physician, the hospital, and the community.

The Joint Conference Committee

The Joint Conference Committee is a discussion committee of the governing board and the medical staff. It has no intrinsic authority; if allowed to become an action group its usefulness will at once be jeopardized.

Purposes: Its purposes, all directed toward better patient care, should be at least three: (*a*) Communications to keep board, staff, and administration cognizant of pertinent actions taken or contemplated by one or the other. These should be reported to the committee even though they do not require action by more than one component of it. Open communications through the Joint Conference Committee will emphasize the importance of prior knowledge of all affected groups before action is instituted and will thus prevent misunderstanding. (*b*) Plans for growth and inevitable change in the hospital organization should be considered by this committee. (*c*) Problems or issues which arise in the operation and affairs of the hospital affecting all parties should be brought to the committee for consideration.

Organizations

While the Joint Conference Committee may be organized in any of several ways the following, which is only a guide, is offered as an example:

(*a*) The Joint Conference Committee of the governing board and the medical staff should be composed of equal numbers of representatives elected or appointed by the governing board and the medical staff. The administrator should be an ex officio member of the committee.

(*b*) The chairman of the Joint Conference Committee may be alternated between representatives of the governing board and of the staff.

(*c*) The Joint Conference Committee should meet at regular intervals no less frequently than four times per year and should meet on call when necessary.

(*d*) The committee should feel free to invite to its meetings persons within or without the hospital who can contribute from their specialized knowledge or experience.

(*e*) A formal agenda should be prepared from suggestions of the members and submitted to all members of the committee in sufficient time before the meeting.

(*f*) Minutes should be kept by the secretary and should be maintained in the permanent records of the hospital.

(*g*) A résumé of the minutes of the Joint Conference Committee should be presented at meetings of the governing board and at meetings of the medical staff.

This statement was approved by the Board of Trustees of the American Medical Association, June 20, 1958, and by the American Hospital Association at its meeting, Nov. 20-21, 1958.

"CRASH" PROGRAM BEGUN BY NIH

A "crash" program aimed at defining the impact of National Institute of Health programs on past and present operations of medical schools is expected to be ready for a first draft report in early February. The final report with recommendations is due for presentation to Congress April 1.

The study results from a congressional directive, and the task is of such import that a new Division of Training in Institutional Relations has been formed and staffed to accomplish the task. Dr. Edward L. Turner, Secretary of the A. M. A. Council on Medical Education and Hospitals, journeyed to Washington last month to confer with NIH officials on the study.

Dr. James Shannon, director of NIH, met last fall with the deans of 20 medical schools to explain the project which will be based on data covering three periods in the schools' history: 1936, 1946, and 1956. The study will cover only 20 schools because of the short time allotted.

NEW PUBLICATIONS OF THE COUNCIL ON MEDICAL SERVICE

Following are new publications of the A. M. A. Council on Medical Service:

The Hill-Burton Study, A Review of the Hospital Survey and Construction Act Since 1946.

A Survey of Union Health Centers, 1958. Prepared by the Committee on Medical Care for Industrial Workers of the Council on Medical Service and Council on Industrial Health.

Report of the A. M. A. Planning Conference on Medical Society Action in the Field of Aging, held in Chicago, Sept. 13-14, 1958.

Report of the Commission on Medical Care Plans, Part 2. Contains statistical appendices and background materials and the results of various surveys and compilations prepared under the supervision of the members of the Commission. Part 1, which will be distributed at a later date, will contain the findings, conclusions, and recommendations of the Commission.

PHYSICIANS TRAVEL FAR FOR STUDY

The mobility of physicians in search of postgraduate education appears to be virtually unlimited. This is one of the early results of a geographically oriented study being made by the A. M. A. Council on Medical Education and Hospitals. Based on data collected for the 1956-1957 academic year, the study covers 55% of the total enrollments reported that year in 65% of the postgraduate courses in 72 cities. Preliminary findings show that many physicians enroll in courses given hundreds or thousands of miles from their homes. A corollary finding is that those states which offer no courses of their own also contribute the fewest physician enrollments to postgraduate courses in other areas. Publication of the study is expected early next year.

QUARTERLY CUMULATIVE INDEX MEDICUS

Volume 59 of the Quarterly Cumulative Index Medicus, covering literature for the first half of 1956, has been mailed to subscribers and is now available for purchase from the Order Department of the American Medical Association. Editing and reproduction of copy for Volume 60 is in progress.

JOURNAL INDEX

The index to volume 168 of The Journal will appear in the Jan. 10, 1959, issue. Those who wish extra copies of the index may receive them, without charge, on request to the Order Department, American Medical Association, 535 N. Dearborn St., Chicago 10.

COUNCIL ON MEDICAL SERVICE

PENNSYLVANIA PUBLIC RELATIONS CONFERENCE LEADS THE WAY

RÉSUMÉ.—Review of current program in Pennsylvania to bring about better distribution of medical care to the entire state. Presentation of the Kansas Plan which has been in action long enough to show what a state can do to increase and improve medical care. First official presentation of the study, "Pennsylvania Rural Physicians—Their Satisfaction with Medical Practice." State and A.M.A. activity in the field of placement service.

The Medical Society of the State of Pennsylvania marked up a first in public relations when John F. Hartman Jr., M.D., member of the state Public Relations Committee, called to order the eighth annual Public Relations Conference. This open session of the 108th annual meeting of the Pennsylvania medical group is the first in the United States to be devoted entirely to Physician Placement Service activities.

Charles J. H. Kraft, M.D., chairman of the Pennsylvania Committee on Rural Health and Physician Placement, reviewed the activity of his committee in this area for the past several years. During this period a comprehensive set of printed forms has been developed for securing pertinent information from physicians seeking a location for practice and from communities seeking a physician. No attempt has been made to "match" the physician with the community, but rather the function of the service has been to provide a source of information for physicians and communities.

"Physician Placement and the Medical School" was discussed by W. Clark Wescoe, M.D., dean of the University of Kansas Medical School. A little over 10 years ago the Kansas Medical Society and the University of Kansas Medical School outlined a cooperative program designed to bring more and better care to the small communities of Kansas. The three-point program aimed toward (1) increasing the size and facilities of the state-supported medical school (this included an active preceptorship program), (2) making postgraduate courses available the year round at the Kansas City Medical Center and even carrying such to the areas where physicians have difficulty in getting away from a solo practice, and (3) establishing an active placement service to work with communities seeking a physician and to bring these to the attention of their medical school graduates as hospital training is completed. No county in Kansas is now without a physician.

The presentation of the four-year study, "Pennsylvania Rural Physicians—Their Satisfaction with Medical Practice" was made by William G. Mather, Ph.D., head of the department of Sociology and anthropology at Pennsylvania State University. This study, made by William G. Mather and Kinzo Yamamoto, draws a parallel between rural-reared and urban-reared physicians in private practice in rural areas of Pennsylvania. ("Rural" is used in the study to connote open country and towns of less than 2,500 population.)

Information was secured from a series of mailed questionnaires, supplemented by personal interviews of a 20% sample. Summarizing charts cover such subjects for the rural Pennsylvania physicians as (1) place of rearing (population-wise), (2) age according to place of rearing, (3) relationship between age and average size of place of office, (4) preferred place of practice (if compelled to move), (5) degree of participation in community organizations, (6) net income, (7) place of practice, and (8) years of practice. Also considered in the study were (1) size of place of rearing of the wife of the physician and (2) the occupational status of the father-in-law of the physician.

A staff member of the A. M. A. Council on Medical Service discussed the "Public Relations Implications of Physician Placement." Emphasis was given to the public relations value of having a physician when and where he is needed. An active placement service is not a guarantee of a physician in every place seeking one, but such a service does make the public aware that an effort is being made on the part of organized medicine to bring about a better balanced distribution of existing medical care.

Specific activities of state medical associations in this area were discussed, such as (1) up-to-date and detailed information on areas seeking physicians for the use of physicians seeking a location, (2) planned field work, (3) statewide community medical rating surveys, and (4) medical school scholarships. Particular stress was given to the importance of the young physician-to-be answering the correspondence of those seeking his services. The public relations value of this factor should not be underestimated.

COMMITTEE ON MEDICAL CARE FOR INDUSTRIAL WORKERS

Compulsory Temporary Disability Insurance Programs.—A new publication entitled "Compulsory Temporary Disability Insurance Programs" was issued in the latter part of November by the Committee on Medical Care for Industrial Workers.

The publication consists of five papers specially prepared at the committee's request by program administrators of the statutory temporary disability programs in the states of California, New York, New Jersey, and Rhode Island and by the United States Railroad Retirement Board.

The articles review the origin and development of each of the programs, describe eligibility and benefit provisions of the various programs under their respective laws, present current statistical information on their experience, and present descriptions of types of administration of the programs.

At the committee's request, each program administrator included in the article submitted for publication a brief review of the role of the medical profession in the administration of the law and, in some instances, described the status of relationships between the administrative agency and physicians in the community as well as local and state medical societies.

Copies of the publication are available, without charge, on request to the Committee.

Joint Committee of the Council on Medical Service and the Council on Industrial Health.

MEDICAL NEWS

CALIFORNIA

Directory of Psychiatrists.—The Southern California Psychiatric Society has recently published a Directory of Psychiatrists and Psychiatric Facilities in Southern California. It is a plastic-bound book listing all psychiatrists in Southern California, both alphabetically and geographically, psychiatric hospitals, clinics, and out-patient departments, including their staffs, eligibility, requirements, etc. Copies are available from the Office of the Society. Please direct inquiries to: Southern California Psychiatric Society, 427 N. Camden Drive, Room 104, Beverly Hills, Calif.

Society News.—The 1958-1959 officers of the California Academy of General Practice are: president, Dr. Carroll B. Andrews, Sonoma; president-elect, Dr. Leon O. Desimone, Los Angeles; secretary, Dr. Clarence T. Halburg, Redlands; treasurer, Dr. John A. C. Leland, Berkeley; executive secretary, William W. Rogers.——The Pan American Medical Association, Southern California Chapter, has elected the following officers for 1959-1960: president, Dr. Salvador Castanares; president-elect, Dr. Ross V. Parks; first vice-president, Dr. Joseph M. De Los Reyes; second vice-president, Dr. Miguel A. Llanos; executive secretary, Dr. Jose P. Badel; assistant executive secretary, Dr. Kenneth B. Jacques; treasurer, Dr. Carl E. Ebert; assistant treasurer, Dr. Milo Ellik; secretary, Dr. Charles J. Lopez; and assistant secretary, Dr. C. Vernon Sanders. The next meeting will be in March, 1959.

Program on Pharmacology and the Mind.—A program on "A Pharmacologic Approach to the Study of the Mind" will be offered Jan. 25-27 at the University of California Medical Center, San Francisco. A staff of more than 40 general practitioners, psychiatrists, and medical scientists will participate. The aim of the program is "to go beyond the usual discussions of drug effects and deal with the questions which must be answered before the so-called mental diseases can be approached successfully with the use of chemical compounds." The program is presented by the University of California School of Medicine and the department of continuing medical education of University Extension in cooperation with the Langley Porter Neuropsychiatric Institute. A special guest will be Aldous Huxley, speaking on "The Final Revolution." Talks and panel discussions will deal with such topics as cerebral circulation, psychochemistry, psychopharmacology, a clinical approach to mental diseases, nonempiric approaches from the basic sciences, problems of research design and clinical evaluation, pharmacology of the tranquilizers, therapy with the tranquilizers, the hallucinogens, stimulants, pharmacology of monamine oxidase inhibitors, therapy with psychic energizers. Program chairmen are Robert M. Featherstone, Ph.D., chairman, department of pharmacology, and Dr. Alexander Simon, chairman, department of psychiatry and medical superintendent, Langley Porter Neuropsychiatric Institute, San Francisco. Information may be obtained from the Department of Continuing Education in Medicine, University of California Medical Center, San Francisco 22.

FLORIDA

Seminar on Cardiovascular Diseases.—The sixth annual seminar on cardiovascular diseases will be held Feb. 19-21 at the Prudential Auditorium in Jacksonville, sponsored by the Northeast Florida Heart Association in cooperation with the Division of Postgraduate Education of the College of Medicine of the University of Florida. The seminar has been accepted for credit by the American Academy of General Practice. The speakers are Drs. Samuel A. Levine, Boston; Irving S. Wright, New York City; Andrew G. Morrow, Bethesda, Md.; Victor A. McKusick, Baltimore; Max Michael Jr., Jacksonville; William J. Taylor, Gainesville; and Myron W. Wheat Jr., Gainesville. This seminar will include recent developments in the diagnosis and treatment of cardiovascular diseases. The formal lectures will be correlated with panel discussions and question periods in which the entire staff will participate. Information may be obtained from Dr. Daniel R. Usdin, Chairman, Cardiovascular Seminar, Northeast Florida Heart Association, 1628 San Marco Boulevard, Suite 7, Jacksonville 7, Fla.

IOWA

Society News.—The Iowa Academy of General Practice has elected the following officers for the ensuing year: Dr. Lewis H. Jacques, Iowa City, president-elect; Dr. Henning W. Mathiasen, Council Bluffs, vice-president; and Dr. Verne L. Schlaser, Des Moines, secretary-treasurer. Dr. Roscoe M. Needles, of Atlantic, was elected to a three-year term as director, and Dr. Ralph H. Moe, of Gris-

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Physicians are invited to send to this department items of news of general interest, for example, those relating to society activities, new hospitals, education, and public health. Programs should be received at least three weeks before the date of meeting.

wold, was reelected national delegate and Dr. George A. Paschal, of Webster City, was elected alternate national delegate, both for two-year terms. Dr. Robert L. Knipfer, of Jesup, was presented the gavel and became president of the chapter for 1958-59; Dr. Donald H. Kast, of Des Moines, the immediate past-president, became a member of the board of directors.

MICHIGAN

University and Hospital Plan Affiliation.—Approval of a proposed affiliation agreement between Wayne State University and Sinai Hospital has been given by the university's board of governors. With the acceptance of Sinai as an affiliate, the College of Medicine now has three private Detroit hospitals available for all phases of teaching, research, and patient care. The other private affiliates are Children's Hospital of Michigan and Harper Hospital. Grace and Detroit Memorial hospitals have had departmental arrangements with the College of Medicine for several years. Public hospitals used extensively by the College of Medicine for teaching are Detroit Receiving, Herman Kiefer, and the Veterans Administration Hospital in Dearborn. Sinai is a 230-bed hospital located in northwest Detroit. Stipulations of the agreement will be maintained through a permanent standing committee appointed jointly.

NEW YORK

Annual Surgical Lecture.—On Feb. 10 the Buffalo Surgical Society will sponsor the Roswell Park Lecture, this year to be given by Dr. Michael E. DeBakey, chairman, department of surgery, Baylor University College of Medicine, Houston, Texas, on "Some Observations on Aortic and Arterial Surgery." Dr. DeBakey will be awarded the society's gold medal, being given for the 12th time in honor of Dr. Roswell Park, professor of surgery, University of Buffalo, 1883-1914. Dr. Gustave P. Milkey, 518 Linwood Ave., Buffalo 9, is secretary of the society.

University News.—Albany Medical College has received a grant of $50,000 from the Kresge Foundation, which will be applied toward the cost of a new eight-story addition to house facilities for teaching and research.

Decrease in Industrial Accidents.—Industrial accidents reported to the New York State Workmen's Compensation Board during the nine months ended Sept. 30 were the lowest in New York State for any similar period since 1941. A total of 483,859 accidents were reported to the board from January through September of 1958. This is 74,435, or 13.3%, less than the 558,294 reported in the first nine months of 1957. The number of deaths reported to the board through September of this year was 1,121, or 9.6%, less than the 1,240 reported in the like period last year. There were 11.5% fewer accidents in the New York metropolitan area in the first nine months of 1958, compared with the same period in 1957. Included in the metropolitan area are the five boroughs of New York City and the counties of Nassau, Suffolk, Westchester, and Rockland. The decline in work-connected accidents reported in the rest of the state for the same periods was 15.7%.

New York City

Foreign Lectures by Grant Recipients.—Three members of the Columbia University faculty will lecture in Australia and Finland during this academic year and next as Fulbright grant recipients. Theodosium Dobzhansky, Sc.D., professor of zoology, is to lecture in 1959-1960 in biology and genetics at the University of Sydney, New South Wales, Australia. Dr. Bernard Raymond Fink, assistant professor of anesthesiology, College of Physicians and Surgeons, will lecture in 1958-1959 on anesthesiology at the University of Turku, Finland. Victor K. La Mer, Ph.D., professor of chemistry, will lecture in 1959-1960 in physical chemistry at the Division of Chemistry, Commonwealth Scientific Industrial and Research Organization, Melbourne, Australia.

Conference on Diagnostic Data Processing.—The possibilities of using the facilities of modern computers to aid in medical diagnosis will be the subject of a conference to be held Jan. 14 at the Rockefeller Institute, New York City. The all-day session will be introduced by Vladimir K. Zworykin, Ph.D., director of the Medical Electronics Center of the institute. Participants in the conference will include medical diagnosticians, computer programmers, electronic engineers, biophysicists, and hospital administrators. The conference will hear reports and consider a number of areas of medical diagnosis and hospital practice where computer use can result in more efficient use of medical facilities, including the gathering and analysis of public health data, the keeping of comprehensive case histories, reduction of the number of laboratory tests, or the automatic requesting of missing tests. Attendance is by invitation.

Programs at Psychotherapy Institute.—A stepped-up program of international exchange of scientific information has been announced by the Postgraduate Center for Psychotherapy. Dr. Lewis R. Wolberg, medical director and dean, said that the center's International Seminars on Mental Health henceforth will be scheduled twice a year instead of annually. The seminars, conceived and financed by the Samuel Rubin Foundation of New York and endorsed by the World Federation for Mental Health, bring to this country scientists from other parts of the world to share their ideas and concepts with leaders of American psychiatry. Dr. Konrad Z.

Lorenz, Viennese naturalist now with the Max Planck Institute in Westphalia, Germany, concluded a recent series with a lecture Oct. 30 at the American Museum of Natural History on inborn reaction patterns of animals. The international seminars are part of the public education program through which the Postgraduate Center for Psychotherapy is attempting to further professional and public understanding of mental health problems and programs. The center provides therapy to about 600 adults and children each week, conducts research, and trains psychiatrists, psychologists, and psychiatric social workers for work in mental health clinics. Dr. Paul H. Hoch, New York State Commissioner of Mental Hygiene, is chairman of the advisory council for the international seminars.

NORTH CAROLINA

Dr. Hohman Honored.—Dr. Leslie B. Hohman, professor of psychiatry, Duke University School of Medicine, Durham, is one of the four physicians who received citations from the National Society for Crippled Children and Adults during the society's annual meeting in November. Dr. Hohman's citation, presented by Gov. Joseph J. Foss, of South Dakota, paid tribute to his "outstanding contributions to knowledge and understanding of the problem of cerebral palsy" and his "more than ten years of continuous and invaluable guidance to the Easter Seal Societies nationwide as Counselor in Neuropsychiatry." Other physicians cited were Dr. Meyer A. Perlstein, pediatrician, of Northwestern University Medical School, Chicago; Dr. George G. Deaver, professor of clinical rehabilitation and physical medicine, New York University Medical College, New York; and Dr. Winthrop M. Phelps, medical director of the Children's Rehabilitation Institute in Reisterstown, Md. All four are past-presidents of the American Academy for Cerebral Palsy and have been medical counselors to the Easter Seal Society. Dr. Hohman served last year as president of the American Psychopathological Association and in 1956-1957 as president of the North Carolina Society for Crippled Children and Adults.

OHIO

Dr. Hosler Visits U. S. S. R.—Dr. Robert M. Hosler, Cleveland, arrived in Moscow Sept. 12, following an invitation by Dr. V. A. Negovsky, Russian physician whom Dr. Hosler cited in his technical manual on cardiac resuscitation and which led Dr. Negovsky to write to Dr. Hosler. The nine-day trip included a visit to the Institute of Resuscitation, of which Dr. Negovsky is the director.

Personal.—R. O. Jones, M. P. H., of Bradenton, Florida, has been named commissioner of the Muskingum and Guernsey County Health departments to succeed the late Dr. Martha Margaret O'Neal.

PENNSYLVANIA

Prescription Blank Bears United Nations Symbol.—A prescription blank imprinted with a modified United Nations emblem reportedly is being used for the first time by Dr. Richard S. Troxel, Allentown. Permission to use the United Nations emblem with the initials "UN" above and the affirmation "We Believe" below has been granted to Dr. Troxel as a participant in the committee's program designed to enlist the support of all professions and business in behalf of the United Nations. This emblem is also being used on personal and business letterheads, as a public service "drop-in" in national advertising, and at the passenger entrance of commercial aircraft. The President of the United States annually appoints the chairman of the United States Committee for the United Nations, a privately supported citizens organization, now in its tenth year of activity, whose purpose is to "arouse interest in and disseminate facts about the United Nations."

Personal.—Dr. William P. Yant, director of research and development for Mine Safety Appliances Company, Pittsburgh, has received the Arthur Williams Award for "outstanding contribution to the conservation of human life." The event marked the 18th presentation of the award, given in honor of the late Arthur Williams, for many years president of the American Museum of Safety.

Philadelphia

Grant for Research Building.—The National Institutes of Health, Education and Welfare has granted Hahnemann Medical College $882,000 for the construction of a clinical research building. The grant was made with the proviso that it be matched by private funds. Grants for research at the medical college total $800,000 annually, for more than 125 separate investigations. The proposed new structure would provide 50,000 square feet of space exclusively for research by the departments of medicine, surgery, pathology, pediatrics, psychiatry, radiology, obstetrics, and gynecology, and would more than double the current research facilities at Hahnemann. The Clinical Research Institute building would replace the present Elkins Building, erected in 1901, situated between the main College building, facing on Fifteenth Street, and the Hospital, facing on Broad Street. The Clinical Research Institute building will be the first new structure at Hahnemann since 1938, when the Klahr Auditorium and Building was erected.

Hospital News.—The Anita Porter Clothier Memorial Lobby of the Graduate Hospital of the University of Pennsylvania, completely redesigned and remodeled as a gift in memory of his late wife by Mr. William J. Clothier, was presented to the university at ceremonies Nov. 24. Dr. G. Morris Piersol, dean emeritus of the Graduate School of Medicine, presented the lobby to the university, and it was accepted on behalf of the university by Gaylord P. Harnwell, Ph.D., university president.

Annual Hospital Clinical Conference.—The 11th annual clinical conference of the Wills Eye Hospital Staff and Society of Ex-Residents will be held in Philadelphia at the hospital Feb. 19-21. The Arthur J. Bedell Lecture will be delivered by Dr. Brittain F. Payne on "Complications Following Cataract Surgery." In addition to individual presentations and color television operations, clinical, surgical, and research subjects, the scientific program will include special surgical clinics Feb. 19. That evening there will be a scientific meeting of the Ophthalmological Section of the Philadelphia College of Physicians which will be preceded by dinner. Dr. Raynold N. Berke will be the guest speaker on the subject, "Surgical Treatment of Blepharoptosis." The social activities will include an informal reception Feb. 20. The conference will be concluded by a dinner meeting of the Society of Ex-Residents of the hospital. For information write the Wills Eye Hospital, 1601 Spring Garden St., Philadelphia 30.

TEXAS

Symposium on Cancer Research.—The 13th annual symposium on Fundamental Cancer Research will be held Feb. 26-28 at the University of Texas M.D. Anderson Hospital and Tumor Institute, Texas Medical Center, Houston, under the title "Genetics and Cancer." Co-sponsors are the University of Texas Postgraduate School of Medicine, American Cancer Society, Texas Division, and the Texas State Department of Health. Section topics include fundamental aspects of genetics in carcinogenesis, gene interaction in neoplastic growth, genetic basis of cell resistance, and heredity and human cancer. Papers to be presented by foreign participants are:

Radiation in Relation to Carcinogenesis and Mutation, R. Latarjet, Institut du Radium, Paris, France.

The Plasmagene Theory and Cancer Genesis, C. D. Darlington, Oxford University, Oxford, England.

Lysogeny, Transduction and Cancer Genesis, Elie Wollman and Francois Jacob, Institut Pasteur, Paris, France.

Cytogenetics of Experimental Tumors, George Klein, Karolinska Institute, Stockholm, Sweden.

Relations of the Chromosome Status to the Origin and Progression of Tumors, Albert Levan, University of Lund, Sweden.

The Bertner Foundation Lecture is scheduled for the afternoon of Feb. 27. For information write the M.D. Anderson Hospital and Tumor Institute, Texas Medical Center, Houston 25, Texas.

WISCONSIN

Dr. Moe Gives Rogers Lectures.—The Wisconsin Heart Association presented the Dr. Malcolm F. Rogers Lectures, Nov. 6. Dr. Gordon K. Moe, professor of physiology, State University of New York College of Medicine, Syracuse, spoke on "The Physiologic Basis of Cardiac Arrhythmias."

University News.—Dr. Gernot B. Rath, of Bonn University, Germany, has been appointed visiting professor of history of medicine for the second semester of 1958-59. Dr. Rath studied medicine at the Universities of Marburg, Hamburg, Berlin, and Bonn. He obtained an M.D. degree at Bonn in 1948 and turned then to the history of epidemics, anatomy in the middle ages, and medical writing in the 16th and 17th centuries.

GENERAL

Grants for Research.—Research grants and fellowships totaling $4,237,521 were awarded during the month of October by the National Institutes of Health, the Public Health Service's research center at Bethesda, Md. The bulk of the money ($3,634,177) was in grants for support of research projects, of which more than half were concerned with research in the fields of arthritis, metabolic diseases, and mental health. The grants were made to 146 institutions in 35 states, the District of Columbia, two territories, and seven foreign countries. Research fellowships totaling $603,344 were awarded to 157 U. S. citizens for study in 79 institutions in 30 states, the District of Columbia, and six foreign countries.

American Board of Medical Hypnosis.—The establishment of the *American Board of Medical Hypnosis* has been announced. The board will serve as a certifying body for physicians using medical hypnosis as part of their professional work. In addition to examination and other prerequisites, it will be necessary for certified physicians to possess prior diplomate status in one of the American medical specialty boards approved by the Advisory Board for Medical Specialties and by the Council on Medical Education and Hospitals of the American Medical Association. The president of the American Board of Medical Hypnosis is Dr. Jerome M. Schneck, New York City, and the secretary-treasurer is Dr. Bernard B. Raginsky, Westmount, Canada.

Campaign for Cytodiagnosis.—Information to help communities take advantage of cytodiagnosis as an aid to early cancer detection has been furnished 180,000 practicing physicians by the College of American Pathologists, Dr. Charles P. Larson, president of the college, has announced. A report of *standards and procedures for their part in col-*

lecting cell samples for diagnosis has been sent to doctors, and will be made available to all medical students graduating within the next five years. The compilation of data and its subsequent publication and distribution were made possible by a grant from the National Cancer Institute. Copies of the booklet are available to physicians from the College of American Pathologists, Prudential Plaza, Chicago 1.

Society News.—The officers of the **Southwestern Medical Association** elected Oct. 23-25 are: Dr. Alvin R. Clauser, Albuquerque, president; Dr. Russell L. Deter, El Paso, president-elect; Dr. Howard D. Cogswell, Tucson, vice-president; and Dr. Merle D. Thomas, El Paso, secretary-treasurer. The 1959 meeting will be held in Roswell, N. M.——Elected to office at the business session Nov. 6 of the **American Society of Clinical Pathologists** were: president, Dr. Edward L. Burns, Toledo, Ohio; president-elect, Dr. John J. Clemmer, Albany, N. Y.; vice-president, Dr. Clyde G. Culbertson, Indianapolis; secretary-treasurer, Dr. Coye C. Mason, Chicago; members of the executive committee, Drs. Robert W. Coon, Burlington, Vt., Richard E. Palmer, Alexandria, Va.——Elected to office at the 12th annual meeting of the **College of American Pathologists** were: president-elect (to take office fall, 1959), Dr. Frank C. Coleman, Des Moines, Iowa; members of board of governors, Drs. William G. Bernhard, Newark, N. J., H. Russell Fisher, Los Angeles, Oscar B. Hunter Jr., Washington, D. C., and John F. Sheehan, Chicago.

Information Wanted on Rheumatic Disease Personnel.—Because new units for the study of rheumatic diseases are being established in medical schools in this country and abroad, because there is need for information regarding fellowship and traineeship opportunities in rheumatic diseases in the United States and other countries and regarding potential and available candidates, and because information is needed concerning opportunities for temporary exchanges of personnel between medical schools here and abroad, the American Rheumatism Association has recently established a Committee for the Exchange of Information Concerning Faculty Appointees and Fellows (EICFAF). The committee will be pleased to receive information about fellowship and traineeship opportunities and faculty and other staff vacancies, as well as inquiries regarding available personnel. Such information and inquiries should be addressed to: Dr. Currier McEwen, New York University College of Medicine, 550 First Ave., New York 16.

Accidents Among Children.—Each year, the Metropolitan Life Insurance Company's statisticians report, about 6,000 children from 5 to 14 years of age are killed accidentally. This is 40% of all the deaths in this age range. The next leading cause of death, cancer, takes only a third as many lives as accidents. Motor vehicle accidents account for two-fifths of the deaths. At ages 5-9, three out of five of the motor vehicle deaths are among children run over or hit as they play on or cross streets, highways, and driveways. At ages 10-14, one-fourth of the children killed are pedestrians, and deaths in automobile-bicycle collisions are at their peak. Home is the place of accident in 16% of the deaths among boys and 30% among girls at ages 5-14. One-fourth of the fatal injuries among boys and one-eighth among girls occur in recreational and other outdoor places. Farm accidents account for only 7% of deaths among school-age children, but at ages 10-14, when boys are helping increasingly with the farm chores, 10% of the accidental loss of life among boys occurs on farms. One-fifth of the accidental deaths at ages 5-14 result from drowning. Boys are the most frequent victims, drowning causing 24% of all fatalities as compared with 12% for girls. Drownings increase in relative frequency as children grow older. Only 3% of the deaths are the result of falls. Among boys at ages 10-14 years, 13% of the accidental deaths result from careless use of firearms.

Proctologists Take Convention Cruise.—The component societies which make up the Quadrangular Proctologic Convention—the New England Proctologic Society, New Jersey Proctologic Society, New York Proctologic Society, and the Pennsylvania Proctologic Society (the New York group acting as host this year)—convened aboard the Ocean Monarch Nov. 14-22, "to permit the exchange and the dissemination of scientific knowledge and techniques related to the anus, rectum, and colon." The program included the following topics and moderators:

Anorectal Surgery, Dr. William H. Ramsey, Bryn Mawr, Pa.
Prolapse and Procidentia, Dr. Gaspar Angelo, Cambridge, Mass.
Pruritus Ani, Dr. George Becker, Paterson, N. J.
Colon Surgery, Dr. A. W. Martin Marino, Brooklyn.
Presacral Tumors, Dr. Saul Schapiro, Brooklyn.
The Colitides, Dr. Frederick S. Ellison, Hartford, Conn.
Anatomy and Electromodalities, Dr. Norman L. Freund, Brooklyn.
Proctitis, Dr. Urban R. Finnerty, Montclair, N. J.
Amebiasis, Dr. John R. Keane, Boston.
Submucosal Nodules, Dr. Sydney D. Weston, Brooklyn.

Films on various anorectal and colonic subjects were shown. Each panel was followed by a question-and-answer session. Dr. Norman L. Freund, 163 Ocean Ave., Brooklyn 25, is Secretary of the New York Proctologic Society. Dr. Weston was program chairman.

Swedish Chemist Wins Atomic Award.—Prof. George Charles de Hevesy, of Sweden, has been named winner of the second Atoms for Peace award. The Hungarian-born chemist and teacher was selected unanimously from a list of 111 nominees representing 19 countries. The award was announced by Detlev W. Bronk, president of the Rockefeller Institute and of the National Academy of Sciences, and chairman of the board of trustees of Atoms for Peace awards. Prof. de Hevesy will come to the United States to receive the award at ceremonies to be held in New York City in January. He will receive a gold medallion and $75,000 for "his basic contribution to the peaceful uses of atomic energy in the discovery and development of tracer techniques in chemistry, biology, and medicine using natural and artificial radioactive and stable isotopes and for his continuing work in these fields." The award was created as a memorial to Henry Ford and his son, Edsel Ford, in response to President Eisenhower's appeal at Geneva for international efforts to develop nuclear energy for peaceful purposes. The Ford Motor Company has set aside one million dollars for the awards. The first award was presented to Niels Bohr on Oct. 24, 1957. Since the second World War, Professor de Hevesy has worked in Copenhagen and at the Research Institute for Organic Chemistry in Stockholm, his present home.

Submarine Doctor Receives Gorgas Medal.—Lt. Commander John H. Ebersole, USN, medical officer of the USS Seawolf, one of the nation's first atomic-powered submarines, has received the Gorgas Medal for his role in the development of nuclear medicine. The Gorgas award, consisting of a silver medallion, a citation and a check for $500, was presented at the annual dinner of the Association of Military Surgeons in Washington, D. C. Dr. Ebersole, veteran of the Seawolf's recent 60-day underwater cruise, is the 16th recipient of the medal, presented annually for distinguished service in military medicine. The award is made by Wyeth Laboratories in memory of Surgeon General William C. Gorgas, whose work in controlling yellow fever made possible the construction of the Panama Canal. The citation accompanying the Gorgas Medal reads: "For outstanding work in the field of radiobiology in connection with the U. S. Navy's submarine program. As the first physician trained by the Navy for duty with a nuclear-powered submarine, he organized the medical departments of the first two nuclear-powered submarines, USS Nautilus and USS Seawolf, and has shown that men may work, eat, and sleep in continuous proximity to a properly designed nuclear reactor for extended periods of time." Dr. Ebersole has served as medical officer of the Medical Research Laboratory at New London, Conn.

Support for Medical Scholars.—Grants of over $1,160,000 were announced in the annual report of the John and Mary R. Markle Foundation, covering the period July 1, 1957–June 30, 1958. The largest grant was $750,000 appropriated to medical schools in the United States and Canada toward the support of 25 young faculty members selected by the fund as "scholars in medical science." The scholar program has been the major interest of the foundation for 11 years. During that time 231 physicians in 74 medical schools have received help from appropriations totaling $6,800,000. The scholars chosen this year are teachers and investigators in medical schools at the following colleges and universities: Alberta, Baylor, Buffalo, California (San Francisco and Los Angeles), Colorado, Cornell, Harvard, Johns Hopkins, Kansas, Michigan, North Carolina, Northwestern, Oklahoma, Pennsylvania, Queen's, Saskatchewan, Tennessee, Vanderbilt, Medical College of Virginia, Western Ontario, Western Reserve, Wisconsin, Yale, and Yeshiva. A grant of $30,000 toward the scholar's support was appropriated to each medical school, at $6,000 annually for five years. The fund also appropriated $150,000 to the Association of American Medical Colleges for general development of its program, and $200,000 to Washington University School of Medicine, St. Louis, to train young teachers and research workers in its basic science program. The Markle Foundation was established in 1927 by the late John Markle, Pennsylvania coal operator. Grants of nearly 20 million dollars have been made during the 31 years the fund has been in existence.

Award for Paper on Obstetrics and Gynecology.—The American Association of Obstetricians and Gynecologists has announced an award which shall be known as "The Foundation Prize" and shall consist of $500. Eligible contestants shall include only interns, residents, or graduate students in obstetrics and gynecology, and persons with an M.D. degree, or a scientific degree approved by the Prize Award Committee, who are actively practicing or teaching obstetrics, gynecology, or engaged in research in these fields. No fellow of the association shall be eligible and no candidate securing the award shall be eligible to compete again. Manuscripts must be presented under a nom de plume, which shall in no way indicate the author's identity, to the president of the foundation together with a sealed envelope bearing the nom de plume and containing a card showing the name and address of the contestant. Manuscripts must be limited to 5,000 words, and must be typewritten in double-spacing on one side of the sheet with ample margins. Illustrations should be limited to such as are required for a clear exposition of the thesis. The successful thesis shall become the property of the association, but this provision shall in no way interfere with publication of the communication in the official journal of the association or, failing that, in a journal of the author's choice. Unsuccessful contributions will be returned. Three copies of all manuscripts and illustrations entered in a given year must be in the hands of Dr. Jean Paul Pratt, Henry Ford Hospital, Detroit, president of the foundation, before April 1, 1959. The award will be made at the annual meeting of the association, at which time the successful contestant must appear in person to present his contribution as a part of the regular scientific program, in conformity with the rules of the association. The successful contestant must meet all expenses incident to this presentation. Inquiries should be addressed to the Secretary, Dr. E. Stewart Taylor, University of Colorado School of Medicine, 4200 E. Ninth Ave., Denver.

CORRECTION

Tolazoline and Lymph Node Biopsy.—In the item entitled "Tolazoline and Lymph Node Biopsy" in *the Foreign Letter from Brazil, Dec. 13, 1958 issue* of The Journal, page 2040, the word "prescalene" (the anatomic term and not a drug) should have read "tolazoline" throughout the paragraph.

EXAMINATIONS AND LICENSURE

MEDICAL SPECIALTY BOARDS

American Board of Anesthesiology: *Oral.* Phoenix, April 5-10. All applications already on file. Sec., Dr. Forrest E. Leffingwell, 217 Farmington Ave., Hartford 5, Conn.

American Board of Dermatology: *Written.* Several Cities, Oct. 5. *Oral.* Oklahoma City, Jan. 15-18, 1960. The final date for filing all applications is July 1, 1959. Sec., Dr. Beatrice M. Kesten, One Haven Ave., New York 32.

American Board of Internal Medicine: *1959 Schedule—Written,* Oct. 19. Final date for filing application is May 1. *Oral.* For candidates in the South and Southwest, New Orleans, Feb. 3-6. Final date for filing application was Jan. 1. *Oral.* For candidates in the Midwest. Chicago, April 15-18. Final date for filing application was Jan. 1. *Oral.* For candidates on the West Coast. Final date for filing application is March 1. *Oral.* For candidates on the East Coast, Nov. 6-7, 9-10. Final date for filing application is March 1. *Examination in the Subspecialties. Gastroenterology.* Philadelphia, April 17-18. Final date for filing application is Feb. 1. Sec.-Treas., Dr. William A. Werrell, One West Main St., Madison 3, Wis.

American Board of Neurological Surgery: Examination given twice annually, in the spring and fall. In order to be eligible a candidate must have his application filed at least six months before the examination time. Sec., Dr. Leonard T. Furlow, Washington University School of Medicine, St. Louis 10.

American Board of Obstetrics and Gynecology: *Part I.* Various parts of the United States and Canada, January 16. Candidates notified of their eligibility to participate in Part I must submit their case abstracts within thirty days of notification of eligibility. No candidate may take the written examination unless the case abstracts have been received in the office of the Secretary. *Oral and Clinical.* Chicago, May 8-19. Formal notice of the exact time of each candidate's examination will be sent him in advance of the examination dates. Candidates who participated in the Part I examinations will be notified of their eligibility for the Part II examinations as soon as possible. Sec., Dr. Robert L. Faulkner, 2105 Adelbert Road, Cleveland 6.

American Board of Ophthalmology: *Written,* qualifying test (Part I), Various Cities, Jan. 26. *Oral.* Philadelphia, June 2; St. Louis, Oct. 6-10. Sec., Dr. Merrill J. King, 22 White St., Rockland, Maine.

American Board of Orthopaedic Surgery: *Part I.* Washington, D. C., Denver, Colorado and Rochester, Minn., Mar. 26-27. Deadline for filing application was Nov. 30. *Part II.* Chicago, Jan. 21-23, 1959. Deadline for receipt of applications was Aug. 15. Sec., Dr. Sam W. Banks, 116 South Michigan Avenue, Chicago 3.

American Board of Otolaryngology: *Oral.* Chicago, Oct. 5-9. Final date for filing application is February. Sec., Dr. Dean M. Lierle, University Hospitals, Iowa City.

American Board of Pathology: Boston, April 16-19. Final date for filing application is Feb. 28. Sec., Dr. Edward B. Smith, 1100 W. Michigan St., Indianapolis 7.

American Board of Physical Medicine and Rehabilitation: *Written, Part I,* and *Oral, Part II.* Philadelphia, June 12-13. Final date for filing application is February 15. Sec., Dr. Earl C. Elkins, 200 First St., S. W., Rochester, Minn.

American Board of Plastic Surgery: *Oral and Written.* Boston, May 9-11. Final date for submitting case reports is Jan. 1. Corresponding Secretary, Miss Estelle E. Hillerich, 4647 Pershing Ave., St. Louis 8, Mo.

American Board of Preventive Medicine: *Written. Public Health.* Regional, Apr. 9-11. *Occupational Medicine.* Chicago, Apr. 17-19. *Aviation Medicine.* Los Angeles, Apr. 24-26. Final date for filing application for all three examinations is Jan. 15. Sec., Dr. Tom F. Whayne, 3438 Walnut St., Philadelphia 4.

American Board of Proctology: *Oral and Written.* Philadelphia, September. Final date for filing application is March. Sec., Dr. Stuart T. Ross, 520 Franklin Ave., Garden City, N. Y.

American Board of Psychiatry and Neurology: New York City, Dec. 15-16; New Orleans, Mar. 16-17. Training credit for full time psychiatric and/or neurologic assignment in unapproved military programs or services between the dates of Jan. 1, 1950 and Jan. 1, 1954 was terminated on Jan. 1, 1959. Sec., Dr. David A. Boyd, 102-110 Second Ave. S. W., Rochester, Minn.

American Board of Radiology: *Special Examination.* Cincinnati, Mar. 16-19, 1959. Final date for filing application was Nov. 1. Candidates completing training June 30, 1959 are not eligible for the Spring 1959 examinations. Sec., Dr. H. Dabney Kerr, Kahler Hotel Bldg., Rochester, Minn.

American Board of Surgery: *Written* examinations (Part I) will be held on December 2, 1959 at various centers to be announced later. Candidates are urged to apply several months before completion of training requirements although the closing date for filing applications is August 1. Those completing training requirements after September 30 cannot be considered for the Part I examination in December of the same year. *Part II.* Houston, Tex., Jan. 12-13; New Haven, Conn., Feb. 9-10; Durham, No. Car., March 9-10; San Francisco, April 13-14; Indianapolis, May 11-12; Columbus, Ohio, May 14-15. Sec., Dr. John B. Flick, 1617 Pennsylvania Blvd., Philadelphia 3.

Board of Thoracic Surgery: *Oral.* Los Angeles, April. Final date for filing application is Dec. 1. Sec., Dr. William M. Tuttle, 1151 Taylor Ave., Detroit 2.

American Board of Urology: The oral will be given in Chicago in February 1959. Sec., Dr. William Niles Wishard, Jr., 30 Westwood Road, Minneapolis 26.

GOVERNMENT SERVICES

ARMY

Award for Exhibit.—A gold medal was awarded to an Armed Forces Institute of Pathology exhibit on pathology of ionizing radiation injury to hematopoietic organs which was displayed at the joint meeting of the American Society of Clinical Pathologists and the College of American Pathologists, in Chicago, in November. The exhibit compared the effects of radiation on blood-forming organs in pigs with those following the injection of an artificially-produced isotope (cobalt ^{60} bead) into the spleen and bone marrow of pigs. These experiments were conducted by Col. Carl F. Tessmer, M. C., Chief of Radiation Injury and Radiobiology Section, Armed Forces Institute of Pathology, and Capt. Alexander Horava, M. C.

PUBLIC HEALTH SERVICE

Regular Corps Examinations for Medical Officers.—A competitive examination for appointment of medical officers to the regular corps of the U. S. Public Health Service will be held in various places throughout the United States on April 21-24, 1959. Appointments provide opportunities for career service in clinical medicine, research, and public health. They will be made in the ranks of Assistant and Senior Assistant, equivalent to Navy ranks of Lieutenant (j. g.) and Lieutenant, respectively. Entrance pay for Assistant and Senior Assistant Surgeons with dependents is $7,470 (Assistant grade applicants are assigned the temporary grade of Senior Assistant). Provisions are made for promotions at regular intervals. Benefits include periodic pay increases, 30 days annual leave, sick leave, medical care, disability retirement pay, retirement pay which is three-fourths of annual basic pay at time of retirement, and other privileges. Active duty as a Public Health Service officer fulfills the obligation of Selective Service. Requirements for both ranks are U. S. citizenship, age of at least 21 years, and graduation from a recognized school of medicine. For the rank of Assistant Surgeon, at least seven years of collegiate and professional training and appropriate experience are needed. For Senior Assistant Surgeon, an additional three years, for a total of at least 10 years of collegiate and professional training and appropriate experience, are needed. Entrance examinations will include an oral interview, physical examination, and comprehensive objective examinations in the professional field.

Application forms may be obtained from the Surgeon General, Public Health Service (P), Washington 25, D. C. Completed application forms must be received in the Division of Personnel no later than March 6, 1959.

Nearly Eight Hundred Ninety Million Visits to Physicians.—In the first U. S. National Health Survey publication to provide figures from a full year of nationwide household interviewing, it appears that illness or injury caused the American people to stay home from work, stay in bed, or otherwise cut down on normal activities for about 3,400,000,000 days during the year ending June 30, 1958. Acute illnesses, including acute respiratory conditions, totaled 437,900,000, or an average of about 2.6 illnesses per person. How many of these were caused by Asian influenza is not known. However, the report shows that acute respiratory conditions caused an average of about seven days of restricted activity per person, including days in bed or days lost from work or school. About 47 million persons were injured seriously enough during the year to cause them to restrict their activities for a day or more or seek medical attention. Injuries caused 424,100,000 days of restricted activity, or 2.5 days per person. The importance of chronic conditions is indicated by the fact that circulatory diseases were the cause of 484,200,000 days of restricted activity, which would be the equivalent of about 2.9 days per person. The circulatory diseases rank higher than any other group of chronic conditions in this respect. People visited their physicians 889,900,000 times, or an average of 5.3 times per person.

Commenting on the report, Dr. Leroy E. Burney, surgeon general of the Public Health Service, Department of Health, Education, and Welfare, said: "With this first annual summary, the Health Survey is beginning to produce a comprehensive picture that workers in the health fields have long needed."

NATIONAL SCIENCE FOUNDATION

Information Processing Service.—The National Science Foundation has established a Research Information Center and Advisory Service on Information Processing to be operated jointly by the foundation and the National Bureau of Standards. The new service is designed to bring together research and development data on methods and equipment for the processing of scientific information. It is further designed to foster closer cooperation among groups in industry, private foundations, universities, professional societies, and the federal government concerned with developing and improving methods for rapid and efficient handling of large volumes of information. Initiation of the service is a part of a broad program aimed at improving the quality of scientific information services and shortening the time spent by scientists in searching the literature. Other phases of the broad program include the support of scientific publications, translations of foreign scientific literature, and support of information and data-processing centers.

DEATHS

Coke, Mortimer William, Ellisville, Miss.; Baylor University College of Medicine, Dallas, 1921; physician at the Ellisville State School; died Oct. 21, aged 59.

Cooper, Henry Wilbur, Cleveland; University of Michigan Department of Medicine and Surgery, Ann Arbor, 1900; died in the Lakewood (Ohio) Hospital Sept. 6, aged 87.

Darby, Francis Urban Ⓜ Loreauville, La.; Louisiana State University Medical Center, New Orleans, 1934; from July 1, 1953, to June 30, 1956, served in the medical reserve corps of the U. S. Army; served on the staffs of the Louisiana State University Hospital and Our Lady of the Lake Hospital in Baton Rouge; died in Elgin, Texas, Sept. 21, aged 51.

Davidson, Benjamin Reid, Brawley, Calif.; College of Medical Evangelists, Loma Linda and Los Angeles, 1924; veteran of World War II; died in the Veterans Administration Hospital, Long Beach, Oct. 2, aged 58.

Dillard, Harry Knight Ⓜ Lexington, Ky.; University of Louisville School of Medicine, 1937; veteran of World War II; since 1955 Lexington–Fayette County health officer; in 1952 appointed director of the division of school health at the state department of health and regional director of the county health division in Louisville; practiced in Warsaw from 1946 to 1952; member of the American Public Health Association; president of the Kentucky Public Health Physicians Society; on the staffs of the Good Samaritan and St. Joseph's hospitals; died in the Central Baptist Hospital, Oct. 9, aged 47.

Dwiggins, Horace Greeley Ⓜ Tuskegee, Ala.; born in Kansas City, Kan., March 17, 1909; Meharry Medical College, Nashville, Tenn., 1934; veteran of World War II; certified by the National Board of Medical Examiners; specialist certified by the American Board of Ophthalmology; member of the American Academy of Ophthalmology and Otolaryngology and the Association for Research in Ophthalmology; service member of the American Medical Association; fellow of the American College of Surgeons; consultant at the Alabama State Department of Rehabilitation and the Alabama Sight Conservation Association; since 1942 chief ophthalmologist at the Veterans Administration Hospital, where in 1938 he received a staff appointment in general surgery; served as consultant at the John A. Andrew Memorial Hospital, Tuskegee Institute; died Sept. 30, aged 49.

Field, Ernest Joseph Ⓜ Rochester, N. Y.; Friedrich–Wilhelms–Universität Medizinische Fakultät, Berlin, Prussia, Germany, 1921; member of the American Academy of General Practice; on the staff of the Park Avenue Hospital; died Oct. 21, aged 63.

Flemming, Theodore E., Gardenville, N. Y.; University of Buffalo School of Medicine, 1907; member of the Medical Society of the State of New York; health officer of the town of West Seneca from 1916 to 1948; a founder, vice-president and director of the Ebenezer State Bank; died in the Buffalo General Hospital Oct. 16, aged 73.

Foster, Narvel Howard Ⓜ Gallipolis, Ohio; University of Cincinnati College of Medicine, 1939; died Oct. 22, aged 48.

Friedman, Bernard, New York City; University of Maryland School of Medicine and College of Physicians and Surgeons, Baltimore, 1925; on the staff of the Hospital for Joint Diseases; died Oct. 22, aged 65.

Geisenfeld, Jack David, Madison, Wis.; University of Wisconsin Medical School, Madison, 1957; interned at the Wisconsin General Hospital; died in St. Joseph's Hospital Oct. 2, aged 26.

Gordon, Charles Albert Ⓜ Brooklyn; born in 1883; Cornell University Medical College, New York City, 1905; since 1950 professor emeritus of obstetrics and gynecology at State University of New York College of Medicine at New York City, Brooklyn; clinical professor of obstetrics and gynecology at the Long Island College Hospital from 1923 to 1930, when he became clinical professor of obstetrics and gynecology at the Long Island College of Medicine, where he was professor of obstetrics and gynecology from 1948 to 1950; president in 1924, trustee from 1925 to 1931, chairman of the joint committee on postgraduate education from 1923 to 1943, chairman of the board of trustees from 1932 to 1934, and since 1934 chairman of the committee on maternal welfare, Medical Society of the County of Kings; in 1925 president of the Brooklyn Gynecological Society; fellow of the American Association of Obstetricians and Gynecologists, and the American College of Surgeons, of which he was governor from 1949 to 1954; chair-

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man of the committee on public health and medical education in 1925-1926 and since 1937 chairman of the committee on maternal and child welfare, Medical Society of the State of New York; specialist certified by the American Board of Obstetrics and Gynecology; served as a member of the Board of Hospitals, City of New York; director emeritus of obstetrics and gynecology at St. Catherine's Hospital; consultant, obstetrics and gynecology at St. Joseph Hospital in Far Rockaway, Beth El, Methodist, Greenpoint, Kings County, Maimonides, Flushing (N. Y.) and Wyckoff Heights hospitals; consultant in gynecology, Southside Hospital in Bay Shore; consultant in obstetrics at the Mary Immaculate Hospital in Jamaica and Mercy Hospital in Rockville Centre; died Oct. 30, aged 75.

Harbert, John Parkinson Ⓜ Bellefontaine, Ohio; Eclectic Medical Institute, Cincinnati, 1898; served on the faculty of his alma mater; member of the American Academy of Ophthalmology and Otolaryngology; past-president of the Logan County Medical Society; died Oct. 18, aged 84.

Haselton, Frederick Russell Ⓜ Lieut. Commander, U. S. Navy, retired, Nashville, Tenn.; Emory University School of Medicine, Atlanta, 1918; member of the American Academy of General Practice; veteran of World War I; entered the regular U. S. Navy in April, 1921; retired June 30, 1940; died in the Baptist Hospital Oct. 24, aged 66.

Heath, Arthur G. Ⓜ Shreveport, La.; University of Nashville (Tenn.) Medical Department, 1910; service member of the American Medical Association; veteran of World War I; served as health officer for the City of Shreveport; associated with the Veterans Administration Center; died Oct. 17, aged 70.

Hefferan, Joseph Michael, Danbury, Conn.; Loyola University School of Medicine, Chicago, 1916; veteran of World War I; for many years physician with Ringling Brothers, Barnum and Bailey Circus; died in the Veterans Administration Hospital in West Haven Oct. 19, aged 69.

Horton, Miles Christopher, Pinebluff, N. C.; University College of Medicine, Richmond, 1903; member of the Medical Society of the State of North Carolina; died in the Moore County Hospital, Pinehurst, Oct. 19, aged 83.

Jones, Hyzer William Ⓜ Utica, N. Y.; Syracuse University College of Medicine, 1907; fellow of the American College of Surgeons; member of the founders group of the American Board of Surgery; past-president of the Oneida County Medical Society; director of the Blue Cross Hospital Plan; consultant at the Marcy (N. Y.) State Hospital, Ilion (N. Y.) Hospital, Herkimer (N. Y.) Memorial Hospital, Broadacres Sanatorium, Children's Hospital Home, Oneida County Hospital, and Utica State Hospital; served as president of the staffs of the Utica General Hospital and the Faxton Hospital, where he died Oct. 28, aged 74.

Jones, Paul Leonidas Ⓜ Flat River, Mo.; St. Louis University School of Medicine, 1926; veteran of World Wars I and II; on the staff of the Bonne Terre (Mo.) Hospital; died in the Tampa (Fla.) General Hospital Sept. 26, aged 59.

Keenan, Alexander Stanislaus, San Francisco; University of California School of Medicine, San Francisco, 1898; fellow of the American College of Surgeons; an associate member of the American Medical Association; past-president of the San Francisco County Medical Society; member of the city library commission; from 1927 to 1932 member of the city board of health; from 1941 to 1953 medical director of the city employees' health service system; served on the staff of the Mary's Help Hospital; died Oct. 19, aged 86.

Kennedy, Lucius Carter, Middletown, R. I.; University of Pennsylvania Department of Medicine, Philadelphia, 1898; past-president and vice-president of the Lackawanna County (Pa.) Medical Society; served on the staff of the Scranton (Pa.) State Hospital; died Oct. 19, aged 86.

Kerestes, John Jr. Ⓜ Weatherly, Pa.; Temple University School of Medicine, Philadelphia, 1936; member of the Weatherly Board of Health, serving as its chairman; school physician of the Weatherly Schools for many years; physician at the Carbon County Institution District Home at Laurytown; on the staff of the Hazleton (Pa.) State Hospital, where he died Oct. 1, aged 48.

Kiefer, Rodney Hough Ⓜ Pittsburgh; University of Pittsburgh School of Medicine, 1935; member of the American Psychiatric Association; past-president of the Pittsburgh Neuropsychiatric Society; director of the Allegheny County Behavior Clinic of the Criminal Court; associated with Woman's and Presbyterian hospitals; died in Murrysville, Pa., Oct. 6, aged 48.

Kessinger, Jacob Thomas, Hartford, Ill.; Kentucky University Medical Department, Louisville, 1904; died in the Wood River (Ill.) Township Hospital Oct. 24, aged 91.

Koerber, Paul Ernst Ⓜ Russell, Kan.; Omaha Medical College, 1896; in 1951 was named as the "Man of the Year" by the Russell Junior Chamber of Commerce and the Russell Daily News; cited for his many years of humanitarian work; died in the Russell City Hospital Oct. 6, aged 82.

Kramer, William Ernest Ⓜ West Monroe, La.; University of Pittsburgh School of Medicine, 1914; member of the American Trudeau Society; past-president of the Louisiana Tuberculosis Association; veteran of World War I; formerly on the staff of the Veterans Administration Hospital in Alexandria; served as superintendent of the Pines Sanatorium in Shreveport; superintendent and medical director of the G. B. Cooley Sanatorium; died Oct. 17, aged 77.

Leithead, Charles Ellsworth, Lakeview, Ore.; State University of Iowa College of Medicine, Iowa City, 1895; past-president of the Lake County Medical Society; died Oct. 14, aged 83.

Morrow, Benjamin Francis Ⓜ Lake Worth, Fla.; Fordham University School of Medicine in New York City, 1913; member of the Medical Society of the State of New York and the Industrial Medical Association; practiced in New York City; veteran of World War I; died in the Good Samaritan Hospital, West Palm Beach, Fla., Oct. 27, aged 67.

Movius, Arthur J., La Jolla, Calif.; University of Minnesota College of Medicine and Surgery, Minneapolis, 1904; life member of the American College of Surgeons; an associate member of the American Medical Association; member of the Montana Medical Association; formerly practiced in Billings, Mont., where he was founder of the Billings Clinic, and on the staffs of the Billings Deaconess and St. Vincent's hospitals; died in the Scripps Clinic Oct. 21, aged 80.

Nyvall, Clarence Ambrose Ⓜ Salt Lake City; University of Illinois College of Medicine, Chicago, 1914; died Oct. 18, aged 70.

Parker, Walter Thomas, Owosso, Mich.; University of Michigan Department of Medicine and Surgery, Ann Arbor, 1901; veteran of World War I; served as superintendent and chief of staff of the Memorial Hospital; fellow of the American College of Surgeons; died in Brighton Oct. 20, aged 80.

Pillsbury, Richard Theodric, Salisbury, Md.; Duke University School of Medicine, Durham, N. C., 1957; interned at the Duke Hospital in Durham, N. C.; resident physician at the City Hospital, now known as the Cuyahoga County Hospital in Cleveland; drowned Oct. 26, aged 26.

Quigley, William Sullivan, Boston; Dartmouth Medical School, Hanover, N. H., 1908; died in the Peter Bent Brigham Hospital Oct. 20, aged 72.

Reitz, Thomas Frederick Ⓜ Evansville, Ind.; Washington University School of Medicine, St. Louis, 1921; past-president of the Vanderburgh County Medical Society; served as a member of the city and county board of health; member of the board of managers of the Boehne Tuberculosis Hospital; on the staffs of the Protestant Deaconess Hospital and St. Mary's Hospital, where he died Oct. 24, aged 62.

Reynolds, Bushnell Ray, Bakersfield, Calif.; Eclectic Medical Institute, Cincinnati, 1899; died Aug. 10, aged 82.

Shapiro, Arnold Irwin, New York City; New York University College of Medicine, New York City, 1956; certified by the National Board of Medical Examiners; interned at the Meadowbrook Hospital in Hempstead; resident at the Rockland State Hospital in Orangeburg, N. Y., where he died Sept. 14, aged 26.

Shapiro, Philip Ⓜ New York City; Long Island College Hospital, Brooklyn, 1926; died in the Doctors Hospital Oct. 20, aged 56.

Shreve, June Roy, Greensboro, N. C.; North Carolina Medical College, Charlotte, 1915; died in the Wesley Long Community Hospital Oct. 19, aged 65.

Skeen, Carroll Hallam Ⓜ Columbia, S. C.; Ohio State University College of Medicine, Columbus, 1916; service member of the American Medical Association; served overseas during World War I; at one time practiced in Greenfield, Ohio, where he was on the staff of the Greenfield Municipal Hospital in Greenfield, Ohio; orthopedic surgeon, Veterans Administration Hospital, where he died Oct. 18, aged 65.

Smith, Thomas Clarke, St. Petersburg, Fla.; Bennett College of Eclectic Medicine and Surgery, Chicago, 1905; an associate member of the American Medical Association; died Oct. 31, aged 83.

Spradling, Richard Hargrave, Lincoln, Neb.; Lincoln Medical College of Cotner University, 1904; also a pharmacist; served as physician for Nebraska State Penitentiary and as assistant superintendent at Lincoln State Hospital; died Oct. 20, aged 95.

Stauffer, William M. Ⓜ Allentown, Pa.; Rush Medical College, Chicago, 1931; veteran of World War I; on the staffs of the Sacred Heart Hospital and the Allentown Hospital; died Oct. 20, aged 62.

Stein, Carl Ⓜ Loudonville, Ohio; Ohio State University College of Medicine, Columbus, 1932; member of the American Academy of General Practice; veteran of World War II; on the courtesy staff of the Mansfield General Hospital, where he died Aug. 20, aged 51.

FOREIGN LETTERS

AUSTRIA

Radiation Damages in Japanese Children.—At a meeting of the society of physicians in Vienna, Dr. F. I. E. Loewinger reported on the examination by the Atomic Bomb Casualty Commission on all those children who were available and who were exposed to atom bomb explosions in 1945 whether as children, infants, or fetuses. Of 325 children, whose mothers had been pregnant at the time of the explosion and who were within a radius of 2,500 miles, 19 were found to be retarded physically and mentally. These children, who then were in utero, were at a distance from the place of explosion between 725 to 1,624 miles. Most of them were in the third or fourth month of intrauterine life at the time of the explosion. Sixteen of the 19 mothers had had symptoms of radiation disease. Three children who were mentally and physically retarded were found in Nagasaki in a group of 200 children whose mothers were pregnant at the time of the explosion and who were within 2,500 miles from the ground center.

Nineteen cases of leukemia were found up to 1955 in young persons in whom the disease developed before the age of 19. Of these, 16 were within 2,000 miles of the ground center at the time of the explosion. In nine of these patients alopecia occurred and in five purpura developed after exposure to the explosion. In some persons who were under the age of 19, cataracts were found, which, however, did not interfere with vision and which were visible only with the aid of the slit-lamp. Infectious diseases, including tuberculosis, did not occur more often in those who, as children, had been exposed to the explosion than in children of a control group. The case fatality rate cannot be evaluated statistically yet because of the small number of deaths. All 72,107 infants who were born in Hiroshima and Nagasaki during the years 1951 and 1954 were examined. No genetic sequelas as a result of the radiation were detected in the first generation.

INDIA

Oral Cancer.—P. N. Wahi and co-workers (*Journal of the Indian Medical Association,* vol. 31, October, 1958) studied a series of 750 patients with intraoral carcinoma attending the Radium Institute in S. N. Hospital, Agra. Of these cancer of buccal mucosa constituted 53.6%. Next came cancer of the tongue (31.5%) and the rest involved the palate, gums, lips, and tonsils. The preponderance of cancers of the buccal mucosa was probably associated with the habit of chewing tobacco and keeping the quid in contact with the mucosa for hours. Similarly the frequency in the palate was probably due to the peculiar smoking habit of the people with the lighted end inside the mouth. The average age in these patients was 42.4 years, which is younger than the average age for oral cancers reported among Europeans. This also may be due to the habit among Indians of chewing betel nut, tobacco, and lime at an early age. The ratio of men to women was 2:1. The commonest complaints were increased salivation, local pain, swelling or ulcer in the mouth, and swelling in the neck owing to metastases in the regional lymph nodes. Less commonly observed were inability to open the mouth, difficulty in swallowing, and burning sensation in the mouth. A history of pain referred to the eye, ear, or face was present in 12.8%. The commonest forms were ulcer and cauliflower-like growths. Of the 750 tumors 22 presented as a thickened irregular leukoplakic patch. Most of the more advanced growths showed a tendency to superficial ulceration and bleeding on pressure. A simple nodule was present in 33 patients. The regional lymph nodes were involved in 504, the involvement being unilateral in 336. Submandibular and jugular lymph nodes were principally involved.

Carcinomas of the gums and cheeks were found to be more likely to spread to the regional lymph nodes than those at other sites. Epidermoid carcinoma formed 88.8% of the cases. Other forms were adenocarcinoma, lymphoepithelioma, anaplastic carcinoma, and atypical epithelial hyperplasia (72 cases). The incidence of metastasis increased with the degree of malignancy. Adenocarcinoma and lymphoepithelioma probably metastasized late as none of patients with these tumors showed any secondary involvement. A high percentage of grade 1 carcinomas with a diameter of less than 1.5 cm. had metastasized and there was no correlation between clinical and histological gradings. Most of the patients with oral cancer had poor oral hygiene with tartar covering the teeth and pyorrhea. Dental trauma and irritation of the mucosa during betel nut chewing appeared to influence the incidence of oral cancers. The incidence of the disease was also seen to have a direct correlation with the economic status. There was no marked difference between vegetarians and nonvegetarians but most of the patients subsisted on a deficient diet and belonged to the poorer class. Only 24 patients gave a history

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The items in these letters are contributed by regular correspondents in the various foreign countries.

of having suffered from syphilis and 5% had a positive Kahn test. Most of these had cancer of the tonque. Alcohol did not seem to play any etiological role. A history of tobacco chewing was obtained in 82.2%.

Defense Against Abdominal Injuries.—G. S. Sekhon (*Indian Journal of Medical Research*, vol. 46, July, 1958) stated that when abdominal viscera are damaged as a result of blunt injuries, rupture of the abdominal muscles is rare, while a blow that ruptures the abdominal muscles is too spent to damage the viscera. He studied the factors responsible for the protection of the abdominal viscera in such injuries. The osseomuscular abdominal wall and the mobility of the abdominal organs offer an efficient set of defensive mechanisms. Thus the relatively fixed ends of the small intestines, diseased spleen or liver, and distended stomach or urinary bladder suffer most because of their inability to slip out from the causative blow. Although the adoption of the erect attitude has necessitated fixation of the colon, parts of this structure which are backed by a hard base, and are therefore more exposed to injury, such as the secum, the transverse colon, and the sigmoid, are allowed some mobility as a protection against injury. The vertebral column, against which an abdominal viscus is likely to be damaged, is also resilient in structure and is cushioned by the great vessels which themselves act as hydraulic buffers.

Electromyography.—S. I. Fudel-Ossipova (*Indian Journal of Physiology and Pharmacology*, vol. 2, July, 1958) stated that although electromyography is not essential to study the condition of the nerve cells and the peripheral nerves, it may help to diagnose certain disturbances in the neuron, end-plate, and muscle fiber complex as it provides knowledge about the activity of a motor unit and also indicates disturbances of normal relationships among the different components of the complex. The author performed electromyographic investigations on children with poliomyelitis and Little's disease. Electromyographs were recorded simultaneously on an oscillograph from two muscles (either the same muscle from both extremities or antagonistic muscles, depending on the nature of the disturbance expected) using superficial electrodes on the skin. A number of electromyograms under different conditions of excitation of the muscles were taken to get a correct idea of the activity of the neuromuscular apparatus. A normal muscle at rest gives no electrical discharge but when the innervation is disturbed various kinds of electric potentials appear even during the period of rest. A muscle deprived of innervation shows spontaneous fibrillations of low voltage, disappearance of which is a sign of renervation. Besides fibrillation, during the rehabilitation period of poliomyelitis, spontaneous twitchings of bundles of muscle fibers during rest were noticed which varied in frequency and strength. Similar spontaneous discharges were observed in states of regeneration of nerve elements which indicated an increased excitability of muscles associated with growing of new nerve fibers into the muscles. The appearance of such spontaneous activity of muscle fibers in poliomyelitis indicates a favorable prognosis.

When the muscles are rigid as in Little's disease, the electrical activity is of a different kind. The electromyograms usually show incessant oscillations of a low voltage. The smaller and more frequent the oscillations, the stronger the muscle spasm. Thus in both conditions electrical discharges occur in the muscle even in the absence of activity. In poliomyelitis, they indicate a good prognosis and the greater the number of discharges the better the chances of complete recovery, while in Little's disease such electric potentials indicate muscle spasm and the greater the number of discharges the worse the condition and the less the chances of complete recovery. In the latter condition action potentials from the antagonistic muscles were equal in strength so that from the electromyograph itself it was difficult to know which muscle was functioning. Due to increased excitability of the motor neurons, the process of excitation spreads to the muscle of the other extremity which also shows electrical activity along with the contracting muscle. Such irradiation of excitation may spread widely, leading to development of increased excitability in a large area of the spinal cord during the period of recovery. Electromyograms of spastic muscles as in Little's disease have a characteristic appearance consisting of a great number of weak oscillations with almost complete absence of strong oscillations.

Needle Biopsies of the Kidney.—Sarin and Sarin (*Journal of the Indian Medical Association*, vol. 31, Oct. 16, 1958) analyzed 120 aspiration biopsy specimens from the kidney. The biopsy was made in the sitting position by means of the technique of Iversen and Brun. Hemorrhagic diathesis was ruled out prior to performing the biopsy by determining the bleeding time, clotting time, and prothrombin time. The biopsy was performed under local anesthesia. All the patients in whom the renal biopsy was successful had microscopic hematuria for 24 hours and mild backache; eight developed gross hematuria and all of them had diabetes mellitus without hypertension, but there was no constant pathological lesion in the kidney associated with such gross hematuria. In one patient the hematuria lasted eight days but there were no other harmful effects. Although 10 of the patients in this series had chronic pyelonephritis, bacteremia or perirenal abscess did not develop in a single patient. Of the 120 biopsy specimens, 103 showed adequate renal tissue; in 3 only the medulla without the renal cortex was found; 10 showed fibromuscular tissue; and 3 revealed liver tissue. Thus the percentage of successful renal biopsies was 88.3. The diagnosis was definitely established by the biopsy alone in 46 patients with nephrotic syndrome; amyloidosis, chronic lobular nephrosis, pyelonephritis, and Ellis type 1 and Ellis type 2 nephritis accounting for most of these cases.

The underlying pathology of polyarteritis nodosa was discovered by performing a renal biopsy in a patient with pulseless disease. In all these patients renal biopsy also helped in determining the prognosis. Renal biopsy was performed in 36 patients with diabetes under the age of 30 years and revealed microscopic changes in the kidney which have usually been considered rare or infrequent in the young. In 24 patients with pulmonary tuberculosis, 3 were discovered to have renal tuberculosis which was not detected clinically or by laboratory investigations. Others showed focal glomerulonephritis, amyloidosis, or pyelonephritis. Others on whom the biopsy was performed suffered from miscellaneous conditions such as essential hypertension, rheumatoid arthritis, disseminated lupus erythematosus, epidemic dropsy, toxic myocarditis, progressive muscular dystrophy, and respiratory infections. The renal lesions were not identical in all patients who were diagnosed clinically as having essential hypertension; six of these had subacute diffuse glomerulonephritis, nephrosclerosis, and pyelonephritis.

Intravenous Iron Therapy.—K. J. Vyas (*Indian Journal of Child Health*, vol. 7, October, 1958) gave iron intravenously to 30 children suffering from diverse diseases and having anemia. Saccharated iron oxide containing 20 mg. of iron per cubic centimeter of the solution was used. The injections were given daily starting with 0.5 cc. and increasing the dose by 0.5 cc. every fourth or fifth day. The iron solution was diluted with 10 cc. of 5% dextrose solution and given slowly; 30 Gm. of a powder containing 15 Gm. of protein was given orally daily, simultaneously, to enhance hemoglobin formation. The initial values for hemoglobin and erythrocytes were low in all patients, and all the children were undernourished. The probable etiological factor was chronic infection in 23, hookworm infestation in 1, scurvy in 1, hypothyroidism in 1, nephrosis in 1, and early cirrhosis in 3. After the therapy, the hemoglobin value rose in 27 patients. It showed no increase in one patient with rheumatic arthritis and it decreased in two (by 8% in one with nephrosis and by 4% in one with rheumatic carditis). In 13 the rise in hemoglobin per 100 mg. of iron was more than 4%.

The erythrocyte count showed a rise in 24 patients, although the increase was significant in only 8. One patient with pulmonary tuberculosis showed no rise in erythrocyte count, although the hemoglobin rose by 7%. Five patients showed a decrease in red blood cells, in 2 of whom it was also associated with a reduction in the hemoglobin level; 25 patients showed a gain in weight at the end of treatment, 2 did not show any change in weight, and in 3 the weight went down due to loss of edema. The packed cell volume was below normal in all patients. After the therapy it showed a good rise in nine patients, a moderate rise in seven, slight rise in eight, and no rise in six. The mean corpuscular volume increased in 13 patients after treatment. The mean corpuscular hemoglobin was below normal in 21 before treatment, in 19 of whom it returned to normal after treatment while in 2 it showed a further decrease. The mean corpuscular hemoglobin concentration was below normal in 13 patients before treatment, in 9 of whom it returned to normal, in 2 of whom it increased above normal, and in 2 of whom it decreased further at the end of treatment. Toxic reactions developed in seven patients, in three of whom the therapy had to be stopped. These reactions included venous thrombosis, abdominal pain, fever, nausea, pain in the lower extremities, and brown pigmentation with enlargement of the liver suggestive of hemochromatosis. The total amount of iron given to these children varied from 120 to 1,880 mg. in 8 to 35 days, while the total rise in hemoglobin varied from 1.09 to 8.42 Gm. per 100 cc.

Epidemic Encephalitis.—Siddhu and Taneja (*Indian Journal of Child Health*, vol. 7, October, 1958) made a [illegible] study on 12 of 36 children [illegible] eurological residuals observed during an epidemic of encephalitis in Delhi in 1954 and 1955. The investigation was done after a preliminary intramuscular injection of paraldehyde, alone or in addition to phenobarbital. The air was injected in the lumbar spine. The initial injection was 25 cc., a safe procedure, and the further amount of air to be injected was decided from the rate of flow of fluid, the general condition of the child, the clinical impression about the degree of cortical atrophy present, and the age of the patient. A steady flow of cerebrospinal fluid indicated that further air could be injected, but restlessness, vomiting, respiratory embarrassment, and circulatory collapse were indications to stop any further injection. No attempt was made to drain off the fluid completely. The largest amount of air injected was 62 cc. in a 9-year-old child. For six hours after the procedure the pulse, temperature, and general condition of the patient were watched. The youngest child in the series was 9½ months old and the oldest 9 years.

The types of neurological residuals in these children consisted of Parkinsonism in five, mental disorientation in three, and hemiparesis in four. Eleven patients had radiological evidence of corticalatrophy; 4 had widened sulci, 2 had dilated ventricles, and 5 showed both. The air study was successful in all 12 patients. The one who showed no evidence of cortical atrophy suffered from residual paresis in right upper limb, mild cerebellar signs, postencephalitic epileptic fits, and early mental impairment. The degree of cortical atrophy was found to be in proportion to the severity and duration of the disease rather than to the type of the neurological residual. The commonest reactions noticed after this procedure were tachycardia in nine and fever in eight. Tachycardia was usually noticed halfway through the procedure and subsided within a day or two. Fever was noticed within two to six hours and was as high as 107 F (41.6 C) in two patients and 105 F (40.5 C) in two others, while in the rest it varied between 101 and 103 F (38.3 and 39.4 C). Both patients with a temperature of 107 F had residual hemiplegia. No correlation was noticed between the age, the amount of air injected, and the severity of the febrile reaction. Fever persisted longer than any other type of reaction after pneumoencephalography. Other reactions included vomiting, restlessness, tremors, perspiration, and headache. Three patients had no reaction. Maximal reactions occurred within the first 24 hours. The changes on pneumoencephalography were seen to be most marked in patients with gross mental disorientation and in those with severe progressive Parkinsonism.

Health Work in South East Asia.—The South East Asia Regional Committee of the World Health Organization in its 11th session in the regional headquarters in New Delhi in September approved health programs to be carried out in the region during 1960, which will involve an expenditure of more than $7,800,000. The committee (1) decided to set up a South East Asia Center for the classification and study of diseases, (2) recommended that the governments of the region set up epidemiological units in their public health departments, (3) requested the regional director to assist governments in reaching their objectives regarding teaching and training in preventive and social medicine to undergraduate and postgraduate medical students and to medical and health workers, (4) recommended that the governments of the region be requested to make such contributions as possible to the Malaria Eradication Special Account, (5) urged the governments of the region to undertake systematic smallpox vaccination and revaccination programs in an effort to obtain total coverage of the population, and (6) requested the regional director to explore all possible ways and resources to give help to governments and to stimulate environmental sanitation schemes—particularly those aimed at the provision of potable water supplies and the proper disposal of human wastes.

UNITED KINGDOM

Resin-Bonding of Fractures.—Dr. Bernard Block, of the Sydney (Australia) Hospital, reported the successful use of adhesive resins in the bonding of fractures. Studies on the fractured cannon bone in sheep showed that this could be united with epoxyresins and that the bone grew by normal callus formation. Subsequent laboratory testing of the healed bone proved that the resulting repair was very strong. Radioactive isotope investigations made on resin-bonded fractures in sheep and horses proved that the resins were nontoxic and were not absorbed. The technique was then applied to the union of human fractures. An intramedullary polyethylene plug was first prepared and inserted internally to bridge the fracture. The plug was shaped to fit the medulla and softened by heat until it just filled the cavity. A thick adhesive resin was then applied externally to the bone. Glass fiber laminates, impregnated with thin resin to make them adhesive, were wound round the fracture site and a final coating of Fiberglas cloth applied to make a smooth finish. Ground bone meal was used as a filler. Heating by an inert gas for a few minutes caused the resin to gel quickly. The bone about 1½ in. above and below the fracture was treated with the resin. So far only three patients have been treated by this new technique. All obtained a good result. Fractured arms could be used freely after two days and full weight bearing on fractured legs was possible after four days. The epoxyresins are made from diphenylpropane epichlorhydrin, the resulting liquid being converted into a solid by a hardener, which is usually an organic amine, such as diethylene triamine or piperidine. Because complete evaluation of the method and the toxicological hazards will take several years, Block is treating only those patients who present orthopedic problems and hazards. The technique is intended for fresh major fractures as it allows complete mobility of the limb and early weight bearing.

Possible Causes of Leukemia.—The records of the Ministry of Pensions and National Insurance were examined by Abbatt and Lea to discover factors that might cause leukemia (*Lancet* 2:880, 1958). These were used only when they antedated any symptoms which could be referred to the disease. Records of 679 patients with leukemia and of a corresponding number of controls suffering from other diseases were examined. The patients were divided by age of onset into groups of 15 to 24, 25 to 34, and 35 years and over, and by years of onset, from 1940 onward. The investigation provided no evidence that trauma (including fractures), antibiotics, or chronic sepsis were related to the onset of leukemia. It did show some association between the disease and rheumatic conditions and exposure to radiation. The authors previously showed that radiation given for the treatment of ankylosing spondylitis might be associated with an increased incidence of leukemia. In the present study the rheumatic conditions included diseases other than ankylosing spondylitis. Lymph-node involvement and enlargement of the spleen were found in a number of patients with rheumatoid arthritis, and the association of leukemia with rheumatic disease was therefore not surprising. The nature of the association is not known.

Skin Test for Thyroid Disease.—Some patients with thyroid disease, particularly those with struma lymphomatosa, have circulating antibodies which react in vitro with components of human thyroid tissue. Buchanan and co-workers showed that an intradermal injection of a saline extract of human thyroid gives rise to a localized skin reaction in patients whose serum contains thyroid antibodies (*Lancet* 2:928, 1958). A sterile saline extract was prepared from the surgically excised thyroid of a thyrotoxic patient and injected into the volar aspect of the forearm of 33 patients with thyroid disease and 19 controls. Precipitation tests were also made. Strongly positive skin reactions characterized by both erythema and induration were seen only in those patients with thyroid disease who had circulating thyroid precipitins. In general positive skin reactions were observed in patients with struma lymphomatosa or with primary myxedema. With one exception positive reactions did not occur in those without clinical evidence of thyroid disease. The addition of cortisone acetate to the inoculum tended to increase the size of the reaction. The findings show that thyroid antigen is capable of producing an abnormal tissue reaction in patients with thyroid diseases who have an autoimmune etiology.

Iproniazid in Angina Pectoris.—Towers and Wood treated 40 patients who had severe angina pectoris from occlusive coronary atherosclerosis with iproniazid (*Brit. M. J.* 2:1067, 1958). The drug was given in doses of 50 mg. two or three times daily, the only other medication being glyceryl trinitrate and anticoagulants if these appeared to be needed. Most of the patients began to improve within five days to one month after starting treatment, the average period being about two weeks. After one month's treatment 17 of the 40 patients had anginal pain only occasionally, and much greater effort than formerly was required provoked it. A further 14 were improved but still had angina on moderate effort. Only four patients failed to benefit. After three months the electrocardiogram showed improvement in all but six of the patients. Side-effects, which were prominent, necessitated stopping the iproniazid therapy in four patients. The commonest side-effects were giddiness, which was often quite severe, syncope associated with a fall in blood pressure, impotence, and euphoria. Four patients showed a rapid gain in weight owing to a voracious appetite. The authors stated that iproniazid acts by blocking pain impulses and not by improving the coronary circulation. This might encourage the patient to be more active and so precipitate infarction. The drug is therefore not recommended for patients with mild angina. The toxic effects of iproniazid were commented on by Benaim and Dixon, who gave it to mental patients for its euphoric effect (*Brit. M. J.* 2:1068, 1958). They stated that it was hepatotoxic. Two patients who had jaundice with hepatocellular damage and one who had severe cerebral irritation and excitement were observed among 61 patients under treatment with the drug.

Ulcerative Colitis.—Truelove treated ulcerative colitis with hydrocortisone hemisuccinate sodium applied topically (*Brit. M. J.* 2:1072, 1958). The results of a previous trial were encouraging but the conclusions were based rather on personal impressions than on a controlled investigation. In the first part of the trial a comparison was made between the results obtained by applying the drug as a nightly rectal drip and those with an inert preparation resembling it in appearance and given in the same way. The nightly dose was 100 mg. At the end of one week of treatment the patients receiving hydrocortisone therapy showed a striking improvement over those on the inert preparation, not only subjectively but also in regard to sigmoidoscopic appearances and the histology of colonic biopsy specimens. All patients were then treated for two weeks with topically given hydrocortisone hemisuccinate sodium and antibiotics. About 75% were in clinical remission at the end of this time. The addition of an antibiotic was beneficial to only a small proportion of patients and produced exacerbation of symptoms in some. Twenty-six patients who were in clinical remission after this trial were then given week-end maintenance therapy for six months with a view to preventing relapse. This consisted of a rectal drip of hydrocortisone given on two consecutive nights to half the patients, the other half receiving an inert preparation. The clinical course of the two groups was identical, about 40% going into remission, thus proving that such maintenance therapy is ineffective in preventing relapse. The author concluded that topical corticosteroid therapy is better than systemic on account of the rapidity of response and the absence of systemic side-effects. A similar controlled trial, with restricted sequential analysis, was made independently by Watkinson, who came to the same conclusions (*Brit. M. J.* 2:1077, 1958).

CORRESPONDENCE

NEED FOR A LIBRARY OF MEDICAL AUDIOVISUAL AIDS

To the Editor:—A pressing need in the field of medical education lies in the creation of a central agency for the purpose of collecting, constructing, exhibiting, indexing, and lending medical audiovisual aids. Such aids have become the bedrock of medical teaching. They include graphic mediums such as x-ray films, photographs, paintings, slides, motion pictures, charts, diagrams, stamps, electrocardiogram, electroencephalograms, myograms, and three dimensional objects such as anatomic and pathological specimens, models, moulages, statuary, instruments, and drugs. This type of institute would not be a museum in the conventional sense but would be a library of audiovisual aids, relating also to dentistry, pharmacy, nursing, and veterinary medicine. The exhibits, being portable, could be lent to physicians, medical schools, medical societies, school groups, public meetings, and even international exhibitions. Exhibits and important teaching materials, such as the famous kidneys described by Richard Bright, now at Guy's Hospital in London, could be borrowed from foreign institutions and circulated about the United States in the same manner as art treasures lent by museums abroad. A certain amount of loss and breakage would be expected incident to transportation, but the price would be cheap if medical standards could be raised.

Such educators as Dr. Thomas Hull and the late A. J. Carlson have been grieved for at least 20 years over the waste that occurs when medical exhibits of superior quality are disassembled at the close of the annual medical meetings. Such exhibits are seldom used again but are discarded. We are equally negligent in our failure to catalogue the teaching materials of various institutions.

No less significant, as Gerald Gruman has recently indicated, is the loss of invaluable historic materials left by recently deceased leaders of medicine, materials which are lost over the auctioneer's counter or cast into a garbage heap. It is indeed a pity that no guardian-agency exists with an interest in preserving these materials for future use. Physicians of coming generations will certainly reproach us for our negligence and take us to task for our apathy.

The home-building of such an institute might consist of three sections: a storage section, a lending section, and an exhibit section. Farsighted visual educators such as Tom Jones visualize that the exhibit section would contain teaching devices showing medicine in its entirety, emphasizing basic as well as clinical medicine, historic as well as modern, and functional as well as organic. It would show the relationship of a single organ to the patient as a whole and of the patient to the world at large and would aim at integrated teaching. It would consist of a number of wings, each wing devoted to a specific system of organs, and containing books and audiovisual aids relating to that system. If the student were studying, for example, diseases of the lungs, he would enter the lung room to study the books relating to this organ, observe preserved specimens and microscopic slides, peer through the bronchoscope at tumors and ulcers, and observe the technique of lobectomy as shown by models and moving pictures. He would listen to phonograph records of rales, friction rubs, and murmurs. He would examine living cultures of the pneumococcus, tubercle bacillus, or Histoplasma capsulatum. He would see the positive skin test of tuberculin or sarcoid protein. He would study roentgenograms, temperature charts, and spirometric data. He would observe the devices used in the physiological laboratory for the study of pulmonary function. He would smell the putrid odor of lung gangrene or obtain the spongy feel of healthy lungs. He would handle the atomic model that shows the chemical structure of such substances as para-amino salicylic acid. He would listen to tape recordings of lectures on the lungs. He would be inspired as envisioned by the late David J. Davis and the late Arno B. Luckhardt with the statuary, memorabilia, and writings of such historic personalities as Auenbruggher, Laennec, Louis, Skoda, and Evarts Graham. What type of instruction could be more effective?

These ideas are by no means new. They were taught by John Hunter, Jonathan Hutchinson, Joseph Hyrtl, John Billings, William Osler, and Maud Abbott. They were formally subscribed to by a group of medical educators from Chicago who established a Chicago museum of medical sciences which has operated on paper over the past eight years. The institute, as here described, exists, but like the hewn parts of the body of Osiris, is scattered everywhere. The private museums such as the Mutter Museum of Philadelphia, the Warren Museum of Boston, the Cleveland Health Museum, the Hall of Fame of the International College of Surgeons in Chicago, and others, each with eminent collections, specialize in certain segments of medical knowledge, but no one of them shows medicine in its entirety, and none has as a primary object teaching through lending. What is needed is organization, the means of bringing materials together under a single roof. The vastness of the project suggests that a governmental agency undertake it. The Museum of the Armed Forces Institute of Pathology, splendid as it is in its appeal to the public and to the profession, cannot be expected to broaden its scope, since its function is primarily military. Perhaps the National Institutes of Health can be encouraged to meet the demand.

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ORAL HYPOGLYCEMIC AGENTS

To the Editor:—Since the advent of the oral hypoglycemics the physician has been lulled into a sense of security that he will not have to be concerned about potentially dangerous reactions, despite one documented report of a fatal hypoglycemic reaction (McKendry, *Canad. M. A. J.* 76:572-573 [April 1] 1957). While not denying the importance and scientific contribution of the oral hypoglycemic agents, we feel it should be emphasized that clinical hypoglycemic episodes may be caused in a situation where the patient is eating poorly, as with a patient on insulin therapy, and we would like to record briefly a recent experience we have had.

The patient was a 76-year-old woman, admitted to the staff medical service of University Hospitals on Oct. 26, 1958, with a chief complaint of being semistuporous for four hours. She had multiple myeloma, diagnosed in June, 1958, for which she had been placed on prednisone therapy. While she was on this therapy, evidence of diabetes mellitus appeared; the patient had been started on insulin therapy but after a hypoglycemic reaction had been switched to therapy with tolbutamide, 0.5 Gm. three times daily. Within the two months prior to admission she had received phosphorus 32 for further treatment of multiple myeloma. The prednisone dosage had most recently been maintained at 5 mg. three times daily.

Three days prior to the present admission, the patient began to feel weak and dizzy, and the next day she had several episodes of being transiently unresponsive. She was anorexic and ate nothing on the day of admission but continued taking her medicaments. At admission she was semicomatose, but the remainder of the physical examination, including the neurological part, was unremarkable. The blood sugar level was determined, and the patient was given 20 cc. of 50% solution of dextrose and water. Her condition improved strikingly, and she was able to talk. After administration of 30 cc. more of 50% solution of dextrose and water and 240 cc. of orange juice, she appeared perfectly normal.

The finding of a blood sugar level of 37 mg.% confirmed the diagnosis of hypoglycemia. Careful questioning of family and patient failed to reveal administration of any insulin during this period. The tolbutamide therapy was discontinued, and two days later the patient had a fasting blood sugar level of 234 and the next day 171 mg.%. She was then given a tolbutamide response test of 1 Gm. intravenously with a resulting three-hour fall in blood sugar level from 157 to 101 mg.%. This is the usual response in the stable diabetic.

We are submitting this case of diabetes subsequent to steroid therapy with documented clinical hypoglycemia occurring during tolbutamide therapy of 0.5 Gm. three times daily to call again attention to the fact that present claims of the absence of such reactions are not correct, and, as with insulin, careful regulation to avoid dangerous hypoglycemia must be instituted, especially in the patient with anorexia.

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A SIMPLE PRECIPITATION TEST FOR LUPUS ERYTHEMATOSUS

To the Editor:—The appearance of a new laboratory aid in the differential diagnosis of the collagen diseases usually produces some excitement in the medical profession. This is especially true in the study of disseminated lupus erythematosus, because the only reliable laboratory aid to the diagnosis has been the demonstration of L. E. cells, a finding which may be inconstant and require some skill in performance and interpretation. For this reason, the description of a precipitation test by Jones and Thompson in The Journal (166:1424-1428 [March 22] 1958) proved to be of real interest to physicians. In many hospitals and clinical laboratories it was offered immediately as a diagnostic test. To others, this test represented an opportunity for further study, if only to determine the nature of the precipitate formed and to shed light on the defect responsible for its production.

We have had the opportunity to study this test on the rheumatology service and in a large random group of clinic patients with other diseases. Included in this study were serums from routine blood donors. It appeared from the outset that the methodology of this test was not well defined. Minor variations in the procedure often produced significant changes. For example, the speed of addition of the *p*-toluenesulfonic acid reagent to the serum appeared to govern the presence of precipitate formation and the degree of positivity produced. With a carefully controlled rate of addition the production and degree of positivity could be enhanced in patients with known lupus erythematosus. Furthermore, an increase in concentration of the reagent to greater than 12% in glacial acetic acid enhanced this reaction, within certain limits.

Under the procedure outlined by Jones and Thompson, regardless of the rate of addition of the reagent to serum, the incidence of false-positives in our study of other arthritic disorders was high. These patients showed rheumatoid arthritis, osteoarthritis, and gout. Some had unrelated diseases. When the procedure was then adjusted to produce maximal efficiency in the diagnosis of disseminated lupus erythematosus, the incidence of false-positives increased and included many more healthy persons and patients with unrelated diseases.

The methodology in this test received careful study in our laboratories. Care in its performance must be stressed. More realistically, the high percentage of false-positive reactions must be emphasized. At this time, the usefulness of this test may be only that it has called attention to an interesting protein precipitation reaction which is worthy of further study.

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TRACHEAL FENESTRATION

To the Editor:—I am writing to correct the impressions made by Mayer, Rappaport, and Blazsik in an article on "Indications and Contraindications for Tracheal Fenestration," published in The Journal (168:169-173 [Sept. 13] 1958). The first sentence in this paper reads as follows: "In a preliminary report we recently introduced a new method of treatment of pulmonary insufficiency by a procedure to which we gave the name of tracheal fenestration." This is a mistake, the name was not given by Mayer and Rappaport.

The following is a chronological history of the development of tracheal fenestration. In 1954, Drs. Mayer and Rappaport suggested to me that I begin a series of experiments to perfect a permanent tracheostomy better than the current operation. Funds, animals, and space for experimentation were provided for me at the New York University–Bellevue Medical Center through the efforts of Dr. Mayer. This research proceeded to the point where a satisfactory technique was devised, and I gave the name of tracheal fenestration to this operation. The first article on this procedure was "Tracheal Fenestration," by Rockey, Mayer, and Rappaport, published in *Diseases of the Chest* (30:224-227 [Aug.] 1956). Also, a second article was published by myself alone on the "Surgical Technic of Tracheal Fenestration" in the *American Journal of Surgery* (94:486-489 [Sept.] 1957).

In the first reference of their bibliography, two cases were reported which did not belong to Drs. Mayer or Rappaport; they never had any official connection with the management of these cases in any way, and they saw the patients only occasionally by courtesy of Dr. Blazsik and myself. To date, there have been 17 cases of tracheal fenestration. Two of the patients, cases 14 and 15 (operations done on June 23 and June 26, 1958), are the only ones who were seen by Drs. Mayer and Rappaport preoperatively and postoperatively and were their own patients referred to me for this operation. All the operations were performed by me.

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COUNCIL ON DRUGS

To the Editor:—The practicing physicians of the United States are not taking full advantage of the excellent drug evaluation program of the A. M. A. The scope and thoroughness of this program were not appreciated by me until recently when another physician and myself were guests of the Council on Drugs at its annual meeting. The realization that many physicians are not using the Council's findings as reference prompts this letter. The Council, established in 1906, is composed of 18 members, each an authority in his specialty and carefully selected for the Council. All give unselfishly of their knowledge and freely of their time to make the Council's findings accurate and factual. At biweekly intervals new drugs are evaluated through careful analysis of all data and research information provided by the involved pharmaceutical company. In addition, Council-selected consultants are often asked for their opinions. The result is an unbiased and accurate appraisal of the drug being evaluated.

The drug evaluations of the Council are available to the physician through its reports in The Journal and through the annual publication of the book, "New and Nonofficial Drugs." The busy practitioner, deluged with drug advertising through the mails and frequently confronted by overenthusiastic detail men will be well advised to choose this book as his reference for drug usage. He should also read carefully the reports of the Council on Drugs as published in The Journal. In this day of increasing socialization, it is heartening to realize that under a free enterprising system organized medicine through the years has sponsored such activities as the Council on Drugs dedicated to the promotion of good health.

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MEDICAL LITERATURE ABSTRACTS

INTERNAL MEDICINE

Chronic Pulmonary Disease Due to Atypical Acid-Fast Bacilli. A. G. Lewis Jr., F. P. Dunbar, E. McAlister and R. Cacciatore. South. M. J. 51:1241-1250 (Oct.) 1958 [Birmingham, Ala.].

The authors isolated strains of atypical acid-fast organisms, avirulent for guinea pigs and of varying pathogenicity for mice, from 80 patients with chronic pulmonary disease in 4 state tuberculosis hospitals in Florida. The strains were classified into 3 categories, namely, photochromogens, which are definite pathogenic agents; nonphotochromogens, the pathogenicity of which is still under study; and scotochromogens, which are considered to be saprophytes. All 3 types were isolated repeatedly by sputum culture. Atypical organisms including all 3 types were isolated from resected lung tissue of 8 patients to the exclusion of other pathogenic organisms.

Clinical information was obtained from 37 patients having atypical Mycobacterium organisms in the sputum. Chest roentgenograms obtained from these patients were abnormal. The symptomatology was similar to that of pulmonary tuberculosis. The tuberculin test was positive in 20 patients (54%), was negative in 5 (14%), and was not done in 12 (32%). No definite conclusions could be drawn from the few tests done. Coexisting pulmonary diseases were observed in 19 patients: pulmonary emphysema occurred in 12; asthma, in 4; bronchogenic carcinoma, in 1; silicosis, in 1; and bronchopleural fistula, in 1. Most of the patients were treated with isoniazid, aminosalicylic acid (PAS), and streptomycin. The sputum converted from positive to negative in 17 patients (46%) and failed to convert in 20 (54%). Eighteen patients underwent surgical procedures, including biopsy of the scalene node, segmental resection, lobectomy, lobectomy combined with segmental resection, and thoracoplasty. Three of the 18 patients still had positive sputums after the operation. Surgical treatment in patients with atypical organisms should be approached with considerable thought.

All 3 types of atypical organisms differed from Mycobacterium tuberculosis in multiple characteristics. Increased catalase activity would serve to differentiate these atypical organisms from isoniazid-resistant mutants, and cultural characteristics and results of other laboratory procedures would differentiate them from other pathogenic and frankly saprophytic mycobacteria. In view of the isolation of these 3 types of atypical organisms from sputum repeatedly, from multiple areas of resected lung including both cavitary and nodular lesions, and at autopsy from multiple areas, and in the absence of other demonstrable causative agents, one would conclude that, under certain circumstances, photochromogens, nonphotochromogens, and scotochromogens might cause chronic pulmonary disease which was pathologically, roentgenologically, and symptomatically similar to pulmonary tuberculosis. Susceptibility studies revealed resistance, or partial resistance, of the nonphotochromogens to isoniazid, aminosalicylic acid (PAS), and streptomycin. Drug susceptibility varied in cases of photochromogens and scotochromogens. Susceptibility studies indicated that some of the short-term adjuvant drugs, such as streptovaricin, viomycin, and cycloserine, may be of more value than the major drugs. The common association with coexisting lung disease and the relatively greater occurrence in older persons suggest that organisms not usually pathogenic or of low pathogenicity may under certain circumstances become pathogens and produce chronic pulmonary disease.

Gastric Mucin for the Treatment of Patients with High Serum Cholesterol Level. L. Castellani and G. Bertola. Minerva med. 49:3453-3458 (Sept. 12) 1958 (In Italian) [Turin, Italy].

A preparation of hogs' gastric mucin was administered to 27 patients with high serum cholesterol level, 13 of whom were women and 14 were men. The ages of 11 patients ranged from 40 to 55 years, and the ages of the remainder were 65 and over. The serum cholesterol level of the patients varied between 250 and 385 mg. per 100 cc. Seven patients received a daily dosage of 200 mg. of the preparation, and the daily dosage of the remainder was from 600 to 750 mg. The daily dosage of both groups was divided into 2 doses which were administered before the noontime and evening meals

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The place of publication of the periodicals appears in brackets preceding each abstract.

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for a period of 3 weeks. Serum cholesterol levels were recorded before, during, and after withdrawal of the drug.

Treatment with gastric mucin produced a marked decrease in the serum cholesterol level in all the patients. This change was more pronounced among patients who received the higher dosage of the preparation. Serum cholesterol levels returned to the values recorded before the onset of the therapy within 2 weeks after discontinuance in patients who had received the lower dosage and within 8 weeks after the drug had been withdrawn in patients who had received the higher dosage. No significant difference in variation of the serum cholesterol levels was noted between the sexes. The authors believe that, since the therapeutic effect of gastric mucin is short, a longer period of administration is required in patients with high serum cholesterol level. Absence of intolerance to the preparation is an advantage over the use of heparin or phenylethylacetic acid for the same purpose.

The Epidemiology of Q Fever in Great Britain: An Analysis of the Findings and Some Conclusions. B. P. Marmion and M. G. P. Stoker. Brit. M. J. 2:809-816 (Oct. 4) 1958 [London].

A survey of the literature of Q fever shows a remarkable diversity of the ecology of Rickettsia burneti. Its pattern of maintenance in animal or insect hosts differs strikingly from one part of the world to another, and the particular local variant which has evolved may have much significance for the infection of man. The author cites examples of the more unusual geographical variants of the ecology of R. burneti to emphasize that the history of Q fever is full of paradoxes and surprises and that our understanding of the ecology of the causative agent is still incomplete. Q fever should be investigated in each country where it has been detected. Investigations in Great Britain since 1949 have shown that the disease is widespread in the country. R. burneti has been isolated from the milk of cows and goats and from the placenta and wool of sheep. It has also been isolated from the sheep tick, Haemaphysalis punctata, but not from Ixodes ricinus or Dermacentor reticulatus. There was some evidence of an increased frequency of infection in cattle in areas of Kent with large numbers of sheep and in some sheep ticks.

Attempts to find a reservoir of infection in small wild animals or wild birds were unsuccessful. Serologic evidence of infection was found in chickens, but there are, at present, no grounds for assuming that these birds are an important reservoir of infection in Great Britain. Infection in man was not limited to persons working with animals but was found among all persons of the community. Sporadic cases and outbreaks of Q fever occurred at any time of the year but in the areas studied were commonest from April to July. Studies of the transmission of R. burneti to man have shown that sheep or cows were directly or indirectly the main sources of infection. Good evidence was obtained of the importance of unpasteurized cows' milk as a vehicle of infection.

Thalassemia? K. Ytrehus. Nord. med. 60:1321-1323 (Sept. 11) 1958 (In Norwegian) [Stockholm].

Thalassemia is a familial hereditary disease characterized by more or less marked anemia, pathological appearance of the red blood corpuscles which are low in hemoglobin, and increased osmotic resistance of the red blood corpuscles. The disease occurs particularly in the Mediterranean countries and has also been described in India, China, Thailand, and the Philippines. In northern Europe, Scotland, England, and Germany have reported cases. The disease also appears in a less grave, often asymptomatic form, for which the designation "thalassemia minor" has been proposed. Thalassemia has been counted among the hemoglobinopathies but has possibly more to do with a defect in the formation of the red blood corpuscles than with the hemoglobin synthesis. In 1957 the cases of a brother and sister, members of a half-foreign family, treated in Aker Hospital, presented a picture suggesting thalassemia minor. The electrophoretic hemoglobin determinations excluded the possibility of other hemoglobinopathies. Thalassemia has not previously been described in Norway.

The Association of Hepatic and Renal Disease. F. I. R. Martin and L. I. Taft. Australasian Ann. Med. 7:243-250 (Aug.) 1958 [Sydney, Australia].

The entity known as the hepatorenal syndrome gained considerable prominence 20 years ago. Many writers now believe that the renal lesion in liver failure is a variety of acute tubular necrosis precipitated by shock, hemorrhage, or sepsis; others consider that there is a specific association between the lesions in these 2 organs. The authors apply the term "primary hepatorenal disease" to a syndrome in which the lesion in the kidney follows the development of disease in the liver as cause and effect. "Secondary hepatorenal disease," on the other hand, includes cases in which both organs are damaged by the same systemic agent as in leptospirosis or carbon tetrachloride poisoning. In addition, the liver and kidney may be involved by two different and unrelated diseases. The authors record the clinical, biochemical, and histological features of 7 cases in which renal disease, both glomerular and tubular, followed liver disease. In all cases the diagnosis was confirmed histologically either by biopsy or at autopsy, and in some cases serologic tests for autoimmune complement-fixing antibodies were performed. In addition, the authors review the clinical features and autopsy findings in 32 fatal cases of liver disease with jaundice occurring at the Royal Melbourne Hospital between 1953 and 1955.

Two types of primary hepatorenal disease are presented: (*a*) glomerulonephritis associated with chronic liver disease, and (*b*) renal tubular damage (cholemic nephrosis) associated with jaundice. Glomerulonephritis complicating chronic hepatitis may have an insidious onset and run a prolonged course. An immunological relationship to the hepatic disease may be present in some of these cases. A considerable proportion of cases of obstructive or hepatocellular jaundice are associated with proteinuria, epithelial cells and casts in the urine, and some elevation of blood urea level. This occurs irrespective of such factors as operations, hemorrhage, shock, or sepsis. Histologically, these cases usually show evidence of tubular damage. The causes of this renal damage and their mode of action are not at present understood.

The Clinical Features, Pathogenesis and Therapy of Systemic Lupus Erythematosus. I. R. Mackay. M. J. Australia 2:279-282 (Aug. 30) 1958. [Sydney].

Three aspects of systemic lupus erythematosus are receiving attention at present: (1) the fact that it is relatively common; (2) that, although there may be acute exacerbations, the disease may exist in a mild form and be of great chronicity; and (3) that there may be a wide variety of clinical manifestations. Although it can no longer be argued that a positive result to a L. E. cell test is a conclusive diagnostic criterion for classical lupus erythematosus, the author relied mainly upon this test to delineate the group of patients in whom the diagnosis of systemic lupus erythematosus could reasonably be considered. Sixty-six such cases have been reviewed from among patients admitted to the Royal Melbourne Hospital over a 5-year period, and these fall into 4 categories: (*a*) classical systemic lupus erythematosus, 35 cases; (*b*) rheumatoid arthritis with a positive result to the L. E. cell test, 7 cases; (*c*) chronic hepatitis with a positive result to the L. E. cell test, 14 cases; (*d*) atypical systemic lupus erythematosus, 10 cases.

Systemic lupus erythematosus occurs chiefly in young women. The severity and clinical manifestations vary greatly, but the skin, joints, kidneys, and serous membranes are most commonly involved. A developmental predisposition to systemic lupus erythematosus may exist, and the disease may be initiated by various types of tissue injury. Cases of hepatitis in which the L. E. cell test gave positive results (lupoid hepatitis) were closely studied. The status of this syndrome remains uncertain; it may represent a lupus variant. Evidence is adduced in support of the hypothesis that immunological responsiveness is a factor in the pathogenesis of systemic lupus erythematosus; the high incidence (75%) of positive reactions in the autoimmune complement-fixation test and the frequency of plasma-cell and lymphocytic aggregates in affected tissues are considered significant. The effect of steroid hormones in lupus nephritis was evaluated by serial renal biopsy studies. Severe nephropathies were not improved by the administration of cortisone, but in 3 patients with early lesions clinical and histological evidence of arrest was noted.

Hereditary Elliptocytosis: Family with 3 Cases. P. Hoveid. Tidsskr. norske lægefor. 78:844-845 (Sept. 1) 1958 (In Norwegian) [Oslo].

Hereditary elliptocytosis, first described by Dresbach in 1904, is a relatively rare condition characterized by the oval or elliptical form of most of the erythrocytes. More than 400 cases have been published. As a rule, the condition is an innocent anomaly without symptoms and discovered only on examination of blood smears. Patients with the anomaly are classified in 3 groups, i. e., those without increased hemolysis, those with compensated hemolysis, and those with hemolytic anemia. Inheritance is dominant. The condition is found in all races. The lifetime of the elliptocytes is shorter than that of normal erythrocytes. In the case described, in a youth aged 18 years, the clinical picture agreed with the description of hereditary elliptocytosis. The liver was palpable and roentgenologically slightly enlarged. The Bromsulphalein test gave pathological values on 2 examinations, possibly indicating liver function impairment due to the intensified bilirubin excretion. The patient's family consisted of 8 members, all of whom were examined; only the father and a paternal uncle had elliptocytic blood corpuscles, both without signs of anemia or hemolysis.

The Mechanism of Hypoglycemic Action of Antidiabetic Sulfonamides. S. M. Leites and N. P. Smirnov. Probl. endokrinol. i gormonoterap. 4:3-12 (No. 4) 1958 (In Russian) [Moscow].

Preparation BL-55 (Nadisan) was tested in experiments in vivo and in vitro. It was demonstrated that it depresses the activity of hepatic insulinase in normal and diabetic animals and increases the hypoglycemic effect of administered insulin in normal animals, as well as in those with alloxan diabetes and diabetes after depancreatization. In completely depancreatized dogs and in rabbits with severe alloxan diabetes, BL-55 produces no hypoglycemic effect on single or repeated administration. In mild alloxan diabetes when a part of the insular pancreatic apparatus is preserved, Nadisan has a hypoglycemic effect. These data allow the conclusion that the hypoglycemic effect of BL-55 is caused by inactivation of insulinase and is manifested only in those diabetic animals which are still capable of producing a certain amount of insulin. Increase of the hypoglycemic effect of administered insulin (under the effect of Nadisan) may also be caused by inactivation of insulinase by this preparation.

Dyschondroplasia and Hemangiomata (Maffucci's Syndrome): II. W. B. Bean. A. M. A. Arch. Int. Med. 102:544-550 (Oct.) 1958 [Chicago].

The author described in 1955 (report I) 2 patients with Maffucci's syndrome (for whom progress reports are given here) and an infant with lesions suggesting the same diagnosis. He also surveyed most of the cases reported since Maffucci's report was published in 1881. The syndrome is an inborn error of tissue fabrication, a dysplastic mesodermal anomaly in which angioma, phlebectasia, vascular hamartoma, and dyschondroplasia occur in various combinations, separated in different parts of the body or closely intermingled.

The case which the author now reports concerns a 56-year-old bachelor, who had been forced to use crutches from the age of 6 years. After he had had 9 fractures of the left leg, the extremity was amputated when he was 32 years old. On a visit a year ago to the hospital where the amputation was performed, he learned that, in addition to the dyschondroplasia, a sarcoma had been detected on one of the deformed toes of the amputated leg. His general health had been fairly good. The thyroid was diffusely enlarged, but there were no clinical signs of thyroid dysfunction. There was a deformity of the right arm and hand, and on the left wrist there was an angioma nearly as big as a golf ball; after it was emptied by compression, blood slowly refilled it. On both palms there were rubbery-looking dark venous blebs which were slowly erectile after compression. The patient had an inguinal hernia, and there was some scoliosis. A roentgenogram revealed enlarged hilar nodes and an infiltrate with fuzzy margins in the upper lobe of the right lung. There was a single scrotal angioma, the faintest early sign of the Fordyce lesion. There had been some recent extension of the deformity of the right hand and wrist, with redness, swelling, pain, and shininess of the tense skin overlying the deformed bone and cartilage. Osteosarcoma was suspected, but the patient refused surgical treatment. Almost a year later his condition was reported to be unchanged.

Reviewing the literature, the author mentions among others a case presented by Aimes and Franchebois. These authors also discussed the various aspects of dyschondroplasia: the pure form called Ollier's disease; dyschondroplasia with vascular anomalies, the Maffucci syndrome; dyschondroplasia and cutaneous pigment anomalies; the combination of cutaneous angiomas and birthmarks, with underlying change in the bone, which has been called the Trelat-Monad syndrome of angioma, with unilateral hypertrophy of bone; and the Klippel-Trenaunay syndrome of cutaneous angiomas and varices, with unilateral hypertrophy of bone or Parkes-Weber's hemangiomatous hemihypertrophy. Tapié called attention to the fact that Cruveilhier and Hansen observed examples of the combined lesions before Maffucci. In 1835 Cruveilhier, in his "Atlas of Pathologic Anatomy," portrayed an amputated hand which bore multiple angiomas with phlebectasia and dyschondroplasia of the digits. In 1863 Hansen described a man whose right shoulder was the site of a chondrosarcoma, which had appeared after an injury, and who also had a cavernous angioma and phlebectasia of the right hand.

The author concludes that Maffucci's syndrome, with the occurrence in one person of dyschondroplasia, vascular anomalies, and hamartomas, has now been recorded in at least 41 instances. It produces serious deformities but is compatible with an active life. It may be recognized in early childhood and may continue into late years, though there is a serious risk of neoplasm, particularly sarcoma. Its cause is a mystery. Beyond the surgical correction of deformed bones and amputation, no treatment is known.

Effect of Rice Diet on Diabetes Mellitus Associated with Vascular Disease. W. Kempner, R. L. Peschel and C. Schlayer. Postgrad. Med. 24:359-371 (Oct.) 1958 [Minneapolis].

This report is concerned with 100 consecutive patients who had diabetes mellitus associated with vascular disease and who were treated with the rice diet. They were followed for from 3 months to 11 years, and the average period of observation was 22 months. Nine patients died. The rice diet is a high-carbohydrate, low-protein, low-fat, and low-sodium diet, containing 565 to 570 Gm. of carbohydrate, 20 to 25 Gm. of protein, less than 5 Gm. of fat, and 70 to 120 mg. of sodium per 2,400 calories. It was well tolerated. Average insulin requirements as well as average blood sugar levels decreased. Manifestations of cardiovascular and renal disease, such as hypertension, enlargement of the heart, electrocardiographic abnormalities, azotemia, and proteinuria, improved significantly in the majority of patients. Hypercholesteremia, present in 80 of the 100 patients, decreased in 85% from an average level of 325 mg. to an average level of 227 mg. per 100 cc.

The effect of the rice diet on "specific" diabetic retinopathy (aneurysms; punctuate, preretinal, vitreous hemorrhages; waxy exudates; retinitis proliferans) in 44 patients was as follows: progression of lesions, in 9 patients; improvement in one eye but progression of lesion in other eye, in 7; no change, in 15; improvement, in 13. In 19 patients who had hypertensive, arteriosclerotic, or renal retinopathy (papilledema, hemorrhages, exudates, venous thrombosis), the lesions progressed in 3, did not change in 5, and improved in 11 patients. It is not known what single factor causes the effects of the rice diet on diabetes mellitus and its vascular complications. It contains less sodium, protein, and fat than any other diet used in the treatment of diabetes mellitus. The authors conclude that an attitude of resignation with regard to the prognosis in diabetes mellitus with vascular complications including diabetic retinopathy is no longer justified, since the course of the disease can be favorably changed by treatment with the rice diet.

"Infarctoid Cardiopathy" Produced by Hydrocortisone and Monobasic Sodium Phosphate. H. Selye and I. de Salcedo. A. M. A. Arch. Int. Med. **102:** 551-557 (Oct.) 1958 [Chicago].

Many actions of hormones are not direct but are due to the creation of favorable conditions for the actions of nonhormonal agents. The authors studied this phenomenon particularly in relation to the actions of electrolytes. It was found that the production of nephrosclerosis, myocarditis, and periarteritis nodosa by deoxycorticosterone does not depend upon the direct effects of the hormone but upon its ability to sensitize tissues to dietary sodium chloride. Apparently it is through an essentially similar mechanism that deoxycorticosterone produces favorable conditions for the production of nephrocalcinosis by the concurrent administration of, in themselves, inactive doses of phosphate. A particularly striking instance of the selective conditioning of cardiac tissue for the toxic actions of dietary sodium phosphates (monobasic and dibasic sodium phosphate) recently came to the authors' attention. Rats treated concurrently with certain highly active corticoids (e. g., the 9α-halogenated steroids) and monobasic sodium phosphate invariably succumbed with the clinical manifestations of acute cardiac death. Autopsy regularly revealed in their myocardium large, yellowish, infarct-like necrotic patches. Histologically these lesions resembled the true spontaneous cardiac infarcts of man. This similarity is further emphasized by the fact that sudden exposure to stress can precipitate the development of massive cardiac necroses in rats pretreated with subthreshold doses of monobasic sodium phosphate plus corticoids. On the other hand, the experimental lesion essentially differs from ordinary infarcts in that histologically demonstrable vascular occlusions do not occur in the former. To emphasize both their resemblance to, and their distinctness from, true cardiac infarcts, these lesions have been referred to as an "infarctoid cardiopathy."

The demonstration that the myocardium can be selectively conditioned to inorganic salts raised the hope that the interaction between sodium phosphates and steroids might help to elucidate certain problems of cardiac physiology, as well as the cardiac infarcts which occur without evidence of acute coronary occlusion in man. The authors felt that they first had to establish whether the naturally secreted glucocorticoid of man, hydrocortisone, can also selectively condition the heart to the actions of orally administered sodium phosphate and whether the infarctoid cardiopathy can be experimentally induced in primates. Eighteen female rhesus (Macaca mulatta) monkeys were subdivided into 8 groups. Experiments indicated that treatment with large doses of natural glucocorticoid (hydrocortisone) can so condition the cardiac muscle that it responds to severe neuromuscular stress, with the development of extensive acute myocardial necrosis. Combined treatment with hydrocortisone and monobasic sodium phosphate produces such infarct-like myocardial changes even in animals not exposed to stress. In monkeys pretreated with hydrocortisone plus monobasic sodium phosphate, subsequent exposure to a neuromuscular stress produces particularly pronounced and extensive myocardial necroses.

It remains to be shown whether the various experimental and clinical conditions discussed here are, in fact, due to some closely related metabolic derangement within the myocardium and whether the therapeutic measures that proved effective in the experimental infarctoid cardiopathy could serve as a basis for the development of new therapeutic measures applicable to spontaneous cardiac diseases of man. From earlier experiments on the rat, it is clear that such experimental myocardiopathies can be prevented by magnesium and potassium salts.

Cystic Medionecrosis with Dissecting Aneurysm of Coronary Arteries. A. E. Boschetti and A. Levine. A. M. A. Arch. Int. Med. **102:**562-570 (Oct.) 1958 [Chicago].

The authors report a 45-year-old woman in whom a dissecting aneurysm associated with changes of medial cystic degeneration was confined to the coronary arteries. The clinical picture was that of an acute coronary occlusion with electrocardiographic changes commonly seen in an evolving and expanding myocardial infarction. Even in retrospect there appears to be no clinical clue leading to the diagnosis of coronary dissecting aneurysm. Although some importance has been attributed to a history of physical stress occurring one to several days before the onset of clinical symptoms, the available clinical data in the woman presented here did not bear this out. A review of the literature shows this case report to be the second in which both lesions, i. e., medial cystic degeneration and dissecting aneurysm, were present and confined to the coronary arteries.

Aortic cystic medionecrosis with extension of a dissecting aneurysm into the coronary arteries is rare, but medionecrosis and dissection of coronary arteries independent of aortic involvement is even more rare. The first case of dissecting aneurysm of the left coronary artery with associated changes of cystic medionecrosis was described by Lovitt and Corzine in 1952. The authors describe 3 additional cases in which medial cystic degeneration of coronary arteries was an incidental finding at autopsy. These incidental findings suggest that so-called idiopathic dissecting aneurysm, even of the coronary arteries, may well be due to medial cystic degeneration.

Serum Cholesterol, Electrophoretic Lipid Pattern, Diet and Coronary Artery Disease: A Study in Coronary Patients and in Healthy Men of Different Origin and Occupations in Israel. D. Brunner and K. Lobl. Ann. Int. Med. 49:732-750 (Oct.) 1958 [Lancaster, Pa.].

Previous studies on the relationship between arteriosclerosis and disturbances in lipid metabolism came up against the fact that there is always a considerable overlap in the total cholesterol values in patients with coronary disease and in normal controls. It seemed logical that some other lipid or lipid fraction could serve as a clearer indicator of atherogenic activity. The authors had noted great differences as regards the incidence of arteriosclerotic heart disease in various communities in Israel, the population of which is composed of "Ashkenazi" Jews, who came from Europe, the United States, and South Africa, and of "Sephardi" Jews, from the Mediterranean area and the Middle East. Among the Sephardi Jews the Yemenites are of especial interest. The Ashkenazi Jews showed a high incidence of coronary disease, whereas this disease was almost absent among the Yemenites. Other investigations confirmed the low levels of total serum cholesterol and other lipids among the Yemenites. The authors determined by analytic and paper electrophoretic methods the lipid patterns of a group of patients with coronary disease, of various groups of apparently healthy Ashkenazi Jews in different occupations, and of Yemenite Jews.

The results of these studies suggested that the serum beta-cholesterol levels in milligrams per 100 cc. are a better index of atherogenic activity than is the total serum cholesterol level or any other lipid or lipid pattern combination. Of 74 patients with coronary disease, 40% had normal levels of total cholesterol (the normal upper level being taken as 250 mg. per 100 cc.), but only 10.8% had beta-cholesterol levels of less than 180 mg. per 100 cc. The group of Yemenite Jews examined did not show a single example with more than 180 mg. per 100 cc. of beta-cholesterol. The Yemenite Jews were free of evidence of coronary disease. Among Ashkenazi Jews divided into groups according to occupation, it was found that professional workers (physicians) had significantly higher average beta-cholesterol levels than did manual workers. Since the dietary habits of the Jews of Ashkenazi origin are similar, it seems likely that energy output, which varies so much between manual workers and members of a free profession, is the decisive factor in determining lipid patterns and so possibly the incidence of coronary artery disease. The patients with coronary disease showed a low percentage of alpha-cholesterol, which was independent of the total cholesterol level and/or the beta-cholesterol level in milligrams per 100 cc.

The authors point out that their findings in Yemenite Jews approximate the findings of Bronte-Stewart and associates in African Bantus. Although utterly different in race and way of life, Bantus and Yemenites resemble each other in their lipid patterns, in the low proportion of fat in their diets, and in their immunity to coronary artery disease. The fact that 2 racial groups as different as the Bantus and the Yemenite Jews appear to be immune to coronary artery disease contradicts the supposition that the lipid patterns and the predisposition to coronary disease are due to factors of race or heredity, and supports the hypothesis that they are due to environmental causes.

Long-Term Prophylactic Administration of Tetracycline to Chronic Bronchitics. J. Buchanan, W. W. Buchanan, A. G. Melrose and others. Lancet 2:719-722 (Oct. 4) 1958 [London].

According to Buchanan and associates, chronic bronchitis is an important cause of disability and unemployment in Scotland, being at least 3 times commoner in men than in women. The etiology is complex, including genetic and social factors and the effects of atmospheric pollution and tobacco smoking, but bacterial infection is widely accepted as playing a major role. In order to ascertain whether long-continued tetracycline administration would reduce the incidence of acute exacerbations, the authors conducted a trial on male outpatients who attended for at least 12 months at intervals of 3 weeks. All had clear evidence of chronic bronchitis, with persistent productive cough, undue effort dyspnea, and a history of previous acute infective exacerbations which in many cases had been treated in hospital. No patient had active tuberculosis, and none had recently received antibiotic therapy. Preliminary assessment consisted of a full history and clinical examination, roentgenograms of chest and sinuses, electrocardiography, sputum culture, vital capacity determination, weight measurements, urinalysis, and blood examination, including erythrocyte sedimentation rate. The investigations were repeated at intervals during the trial. At intervals of 6 to 12 weeks, serum tetracycline levels were estimated.

The patients were allotted by random selection to 2 groups; one group received tetracycline in a dose of 250 mg. night and morning, and the other group received lactose in capsules of identical appearance. Twenty-six patients received tetracycline, and 25 received the inert substance. The treated group experienced a statistically significant reduction in the number of exacerbations, compared with the control group. Subjectively, the treated patients were improved and had less cough, with reduction in the volume and purulence of the sputum. More of them gained weight than did the controls. No improvement was found on objective investigation. There were no serious side-effects attributable to tetracycline. Satisfactory serum tetracycline levels were obtained. The authors conclude that this form of therapy is indicated in the long-term management of chronic bronchitis.

Familial Osteoarthropathy of the Fingers. A. C. Allison and B. S. Blumberg. J. Bone & Joint Surg. 40B:538-545 (Aug.) 1958 [London].

The authors report on 2 families with a genetically determined arthritis-like abnormality of the hands, characterized by enlargement and loss of mobility of the proximal and distal interphalangeal joints. Twelve of 18 affected members of the first family and 5 of 11 affected members of the second family were seen. There is no known relationship between the 2 families. The condition begins before puberty, is relatively painless, and is not functionally disabling. It resembles the condition described by Thiemann and appears to be one of a group of conditions in which the epiphyses of the bones undergo avascular necrosis. The appearance of the abnormality is controlled by a single autosomal gene, which manifests itself in nearly all persons who are heterozygous for it. Two of the offspring of a consanguineous marriage between affected persons showed much greater involvement than their siblings. This suggests that they may represent the effect of the abnormal gene in double dose. If this is so, the type of inheritance cannot strictly be regarded as "dominant," since the abnormal homozygote is different from the heterozygote.

Blankets and Infection: Wool, Terylene, or Cotton? H. Schwabacher, A. J. Salsbury and W. J. Fincham. Lancet 2:709-712 (Oct. 4) [London].

Antibiotic-resistant strains of pathogenic bacteria have become a serious problem, particularly Staphylococcus aureus which is able to acquire resistance faster than new and potent antibiotics can be produced. Staph. aureus, phage type 80, made its appearance at the hospital with which the authors are connected toward the end of 1957. It became endemic, and measures taken to eradicate it failed. The hospital laundry disinfected woollen blankets with quaternary ammonium compounds. In examining test blankets, the authors found no staphylococci or streptococci, though Proteus vulgaris and Pseudomonas pyocyanea have survived the process. But the fluff from these blankets seemed to play an important part in the spread of infection, as plates exposed on the wards nearly always revealed numerous colonies of staphylococci around a nidus of fluff. Experiments were, therefore, directed toward assessing (1) the effect of more frequent cleaning and more careful use of woollen blankets and (2) the effect of using a blanket material which would not produce fluff. Two experiments were devised to investigate woollen and non-woollen blankets. In both records were kept of any septic cases on the wards.

The first experiment showed that the use of freshly washed blankets, disinfected with quaternary ammonium compounds, for each patient admitted to a test ward reduced the total bacterial count (and especially that of Staph. aureus, phage type 80) and also decreased cross-infection. The second experiment showed that there was a moderate reduction in the total bacterial count when Terylene blankets were used instead of woolen blankets. But the total bacterial count was reduced more and there was no cross-infection during the time that cotton blankets were used. After the first washing cotton blankets did not produce the fluff which seems to be a major factor in the spread of infection.

The Fibre Composition of Hospital Dust. T. A. Pressley. Lancet 2:712-713 (Oct. 4) 1958 [London].

As part of an investigation of the hospital blanket problem, it was thought desirable to make a direct examination of hospital dust—presumably the vehicle chiefly responsible for carrying bacterial infection to a wound. For this purpose samples were collected in 3 hospitals in the Melbourne area. A preliminary sample of floor sweepings contained a high proportion of heavy debris that would never be air-borne, and sampling from the air at bed height was, therefore, undertaken. All samples of air-borne dust collected in the 3 hospitals consisted essentially of cellulose fibers. Very few wool fibers could be found. Most samples subjected to bacteriological examination contained coagulase-positive Staphylococcus aureus. This suggests that the cross-infection with Staph. aureus is primarily due to transfer of the bacteria by some agency other than fluff from blankets and that, therefore, replacement of wool blankets with those made from other textile fibers, or the application of an oiling technique to blankets only, is unlikely to reduce cross-infection.

Acute Myocarditis After A-Influenza: Two Cases. H. Lisager. Ugesk. læger 120:1330-1331 (Oct. 2) 1958 (In Danish) [Copenhagen].

Of 2 cases of heart disorder of acute origin, one set in during influenza with fulminant course; the other appeared 3 weeks after the start of influenza. In both cases the influenza (type A) was complicated by bronchopneumonia of unknown etiology. There were in both instances cardiac dilatation, tachycardia, low blood pressure, and electrocardiographic changes in the RS-T interval and the T wave. The patients survived. In the first case the picture was somewhat obscured by the acute phase of the main disorder and the active therapy. Because of the marked, rapidly increasing heart dilatation in this case, digitalis therapy was discussed but was not considered to be indicated. In the second case insufficiency symptoms occurred, and, as the course here was, on the whole, more peaceful, careful digitalization was applied with good effect.

SURGERY

Haemorrhagic Infarction of the Sigmoid as a Result of Thromboangiitis Obliterans. J. K. C. Rijsbosch. Arch. chir. neerl. 10:124-133 (No. 2) 1958 (In English) [Arnhem, The Netherlands].

At the surgical clinic of the University of Utrecht a 23-year-old man, who was under treatment, suddenly had felt a violent urge to defecate, associated with profuse sweating. These symptoms were followed by severe lower abdominal pain; vomiting continued, but hardly any stools were produced. There was muscular defense in the left lower abdominal region, but no intestinal peristalsis was observed. Rectal examination was very painful. The condition was diagnosed as pelvic peritonitis of undetermined etiology. During laparotomy a large portion of the sigmoid colon was found to be necrotic. The inferior mesenteric artery was completely obliterated. In the course of resecting the necrotic portion of the colon, it was found that the marginal arcades of the colon were very poorly developed—a fact which necessitated a wide resection. The continuity of the colon was restored by means of an end-to-end anastomosis between the ascending colon and the rectum.

The histological examination of the resected specimen revealed that the changes in the inferior mesenteric artery and its ramifications resembled those described by Buerger in 1924 in the arteries and veins of the lower extremities in cases of thromboangiitis obliterans. The arterial lumens were obliterated by a highly vascular connective tissue or by thrombosis with organization. The cells invading these thrombi, which were characterized by their unusual nuclei, might be compared with the cells regarded by Buerger as deformed angioblasts. Granulation tissue containing giant cells and filling the vessels is believed to be pathognomonic of thromboangiitis obliterans (Buerger's disease). On the basis of the similarity between the histological vascular changes observed in this patient and those found in patients with thromboangiitis obliterans of the vessels of the lower extremities, this condition can be regarded as Buerger's disease showing an unusual localization: the inferior mesenteric artery and its ramifications.

Occlusion of the inferior mesenteric artery does not necessarily produce clinical manifestations, for obliteration of this artery is sometimes found at autopsy in the absence of circulatory disturbances in the regions supplied by this artery. While it has been known that transient abdominal symptoms may occur in the course of manifest Buerger's disease of the extremities, the literature on thromboangiitis obliterans in the mesenteric vessels is scanty. Obliteration of the inferior mesenteric artery generally has few consequences with regard to the circulation in the colon, because a satisfactory development of marginal arcades, as a rule, ensures the development of a collateral circulation. An initially adequate collateral circulation, however, may become inadequate as a result of progressive involvement of the marginal arcades. The symptoms which accompany an infarction in the left part of the large intestine are those of "an acute abdomen." The pain is generally in the left side of the lower abdomen. The history often reveals previous attacks of abdominal pain of obscure etiology (intermittent mesenteric claudication). If the general condition permits, laparotomy is carried out, the colon being resected to well beyond the infarcted part. Recently, embolectomies have been described in cases of occlusion of the superior mesenteric artery; if not completely restoring intestinal vitality, such procedures at least permit reduction of the intestinal resection.

Variation of the Serum Aminopherase (Transaminase) Activities in Surgical Patients. V. D'Abbicco and A. De Tullio. Acta chir. italica 14:539-551 (July-Aug.) 1958 (In Italian) [Padua, Italy].

The authors investigated the quantitative variations of serum glutamic oxalacetic transaminase (SGO-T) activity and of serum glutamic pyruvic transaminase (SGP-T) activity in 52 surgical patients. One group of 20 patients had neoplastic disease which in 10 was either a primary or a metastatic lesion of the liver. The second group, consisting of 11 patients, had various types of liver disease, occasionally accompanied by jaundice. The third group of 21 patients had various other disorders to be treated by surgery. No deviation from normal titers in the serum level of the 2 transaminase activities was observed in the patients of the first group who had a neoplastic lesion of an organ which was not in the digestive tract, although a slightly higher level of SGP-T activity was recorded in one patient with pulmonary carcinoma. Unlike other workers, the authors did not find an increased serum transaminase activity in patients with primary or metastatic lesions of the liver. An inversed proportion of SGO-T to SGP-T activity, as compared with normal titers in patients with metastatic lesions of the liver, was the most striking feature of this study. Elevated levels of serum transaminase activity were established in patients with neoplastic or non-neoplastic disease of the liver accompanied by marked jaundice. There was no deviation from normalcy in the serum transaminase activity in patients of the third group who did not have a liver or neoplastic disease.

Vertebra Plana. A. T. Fripp. J. Bone & Joint Surg. 40B:378-384 (Aug.) 1958 [London].

The author reports 4 cases of vertebra plana in 2 boys and 2 girls who were treated at various hospitals in England between 1935 and 1945. No biopsy was performed. The cases were typical in their mode of onset, symptomatology, and clinical findings. The early roentgenographic appearances were also typical. The patients were treated by a period of recumbency but with no deep roentgenotherapy; recent follow-up showed that in each patient there was a complete relief of symptoms without any appreciable clinical abnormality. A complete skeletal survey was carried out in only one patient, and no other bone lesion was observed. Later roentgenograms showed in each patient almost complete regeneration of the affected vertebra, and in 3 of the 4 patients there was a narrow line of sclerosis (the ghost vertebra) representing the original collapsed and dense vertebral body. It appears that solitary lesions of this type in the vertebra can be self-limiting. A review of the patients suggests that in solitary lesions deep roentgenotherapy is not necessary, provided that the patient can be kept under supervision with repeated roentgenographic examination in order that the process of regeneration can be followed. In view of the possible after-effects of deep roentgen-ray irradiation, it is desirable to limit this to patients in whom it is proved to be necessary. If there is roentgenologic evidence of multiple lesions, a biopsy should be performed on the one that is accessible, and appropriate x-ray treatment instituted.

Second Shunting Operations for Pulmonary Stenosis with Cyanosis Following Failure of Original Systemic-Pulmonary Anastomoses. J. A. Haller Jr. Surgery 44:919-926 (Nov.) 1958 [St. Louis].

Of the 1,500 patients with pulmonary stenosis and cyanosis who were operated on between 1944 and 1957 at the Johns Hopkins Hospital, 266 (group 1) were infants, 514 (group 2) were children between the ages of 2 and 5 years, 478 (group 3) were children between the ages of 5 and 12 years, and 242 (group 4) were over 12 years of age. One hundred nine of the 1,500 patients (34 of group 1, 44 of group 2, 18 of group 3, and 13 of group 4) required reoperation because their original systemic-pulmonary anastomoses became inadequate. The average time interval between the original and the second operation in the 4 groups of patients varied between 3 and 8 years. The highest incidence of shunt failure occurred in the group of infants (up to 2 years of age) in which about 1 in every 7 patients required reoperation. The most common cause of a poor result in this group was thrombosis of the original anastomosis. The prognosis was best for the patients in group 3 in which only 1 patient in 25 required a second operation; in 13 (70%) of the 18 patients in this group who required a second anastomosis, the indication for it was that the patients had outgrown their original shunts which were still patent and functioning well. A Potts-type anastomosis was used for the second operation in 57 (52%) of the 109 patients, but follow-up evaluation after the second operation revealed that the type of anastomosis employed in the second operation did not influence the generally good results obtained by the second operation. Ten patients died during or shortly after the second operation, an over-all mortality rate of 9%. Eighty-three of the 109 patients have been followed for more than 3 months, with an average follow-up period of 3 years; 75 (90%) of the 83 patients are considered to have good postoperative results.

Acute Episodes of Diverticulosis of the Large Intestine. M. Marsiglia. Chirurgia 13:292-296 (No. 4) 1958 (In Italian) [Milan, Italy].

An evaluation is made of the therapeutic results in 43 patients who were operated on during the period from 1946 to 1956 for acute diverticulosis of the large intestine in the surgical emergency department of the clinic with which the author is associated. The average yearly number of operations did not change much in this period, which means that antibiotics have not greatly affected the clinical course of the disease. Diverticula had developed in the pelvic colon in 41 patients and in the transverse colon in 2 patients. There were 14 operative or postoperative deaths (32%) recorded, which included 7 of 19 patients with perforation of the diverticulum, 4 of 12 patients with generalized peritonitis without perforation, 1 of 4 patients with peritoneal abscess, and 2 of 8 patients with intestinal occlusion. The last 2 patients died because of a second occlusion which was not detected during the operation.

The author points out that the operation performed on these patients was a lifesaving measure and it did not resolve the disease. A long history of diverticulosis was known to have existed in 9 patients. Frequent occurrence of subacute episodes of colitis preceding the acute episodes of diverticulosis of the large intestine was traced in the history of the remaining 34 patients. The author therefore suggests an early institution of surgical therapy after a trial of medical treatment in patients with recurrent mild or subacute episodes of diverticulosis in order to prevent the onset of the acute phase of the disease.

Proximal Pancreatectomy in the Treatment of Pseudocysts of the Pancreas: I. Eight Pancreatectomies Because of Fistula. P. Mallet-Guy and J. Michoulier. Lyon chir. 54:707-725 (Sept.) 1958 (In French) [Paris].

Pancreatic fistula as a sequela of external drainage for pseudocysts of the pancreas is a grave, often fatal postoperative complication, frequently requiring a second surgical intervention. Experience with external drainage of pseudocysts through the canal of Wirsung in 5 patients showed that this treatment may have more inconveniences than advantages. The pancreatic pseudocysts are the result of a necrotic or traumatic interruption of the excretory system, most frequently of the duct of Wirsung itself. The collection of fluid is maintained by secretion from the segment on the left side of the pancreas, i. e., the proximal segment. Infection is the usual consequence of the external pancreatic fistula, rapidly leading to a pyopancreatic fistula. Skin lesions caused by the digestive action of the escaping pancreatic fluid constitute a grave complication, appearing in the neighborhood of the fistulous opening. Proximal pancreatectomy, which is particularly indicated in patients with fistulas after external drainage, was successfully carried out in these 5 patients. Repeated and correctly performed external drainage, with continuous suction, assuring disinfection of the sac, and separation of the adhesions would have simplified the operation in many of the authors' patients. An external fistula was observed in an additional patient after incomplete pancreatectomy and was corrected by resection of the caudal segment. Two other patients with internal pancreatic fistulas, located in the gastric cavity, were cured by proximal pancreatectomy. Thus, 8 patients who presented fistulized pseudocysts, complicated by infection and blocked by severe adhesions, were cured by proximal pancreatectomy.

Proximal Pancreatectomy in the Treatment of Pancreatic Pseudocysts: III. Conclusions in 21 Personal Cases. P. Mallet-Guy and J. Michoulier. Lyon chir. 54:742-760 (Sept.) 1958 (In French) [Paris].

Three arguments may be advanced in favor of proximal pancreatectomy in the treatment of patients with necrotic pseudocysts of the pancreas: (1) interruption of the pancreatic excretory duct, which is the cause of the pseudocyst; (2) inflammatory lesions of the proximal segment of the gland; and (3) possible occurrence of epithelioma, the first manifestation of which would be pancreatic necrosis. A survey of 39 patients subjected to proximal pancreatectomy, 21 of whom were the authors' own patients and 18 of whom were reported on in the literature, showed that the operation was performed as a last resort on more than one-half of the patients after external drainage; it was performed on 9 patients because of fistula, on 9 because of recurrence of the syndrome, on 2 after internal drainage, and on 1 after sphincterotomy. There were 2 postoperative deaths and 3 late deaths (1 from a malignant recurrence). The results in the surviving patients, 6 of whom were followed from 3 to 14 years after the operation, were excellent. No relapses were noted in any of the survivors.

Considering these results, proximal pancreatectomy seems to be the treatment of choice for patients with necrotic pseudocysts of the pancreas, because it removes the malfunctioning duct of Wirsung which is the substratum of the disease. Yet the operation cannot be performed in all cases, because it is often difficult and may be dangerous, especially in patients with external pseudocysts of the pancreas. External drainage, with continuous suction, performed before the operation helps to improve the results in such patients. Palliative operations have precise indications, particularly in patients with pseudocysts of the head of the pancreas.

Tuberculosis of the Femoral Neck and Greater Trochanter. R. T. Ahern. J. Bone & Joint Surg. 40B:406-419 (Aug.) 1958 [London].

The author reports on 2 girls and 4 boys, between the ages of 3 and 9 years, with tuberculosis of the femoral neck, who were treated at the Heatherwood Orthopedic Hospital in Ascot, England. Three patients were treated conservatively by bed rest and immobilization with the aid of a plaster cast, and the other 3 were treated by excision of the focus and chemotherapy with streptomycin combined with aminosalicylic acid (PAS) or isoniazid, or both. Tuberculosis of the femoral neck is an uncommon lesion occurring in patients in the first decade of life. Excellent results were obtained in the 3 patients treated by immediate surgical intervention under antibiotic cover.

Eighteen patients, 13 male and 5 female, between the ages of 14 and 75 years, with tuberculosis of the trochanteric bursa and greater trochanter were treated at the same hospital by a "standard method" consisting of combined chemotherapy and radical surgery. An additional 14 patients, 11 male and 3 female, between the ages of 11 and 65 years, with the same condition were treated by other methods. Tuberculosis of the trochanteric bursa and greater trochanter is a chronic disease, and advice is sought for superficial abscess of sinus formation. While the disease remains deep to the fascia lata, it is often silent or causes only minor symptoms. The evidence is overwhelming in favor of spread of the disease from bursa to bone. Eight of the 18 patients treated by the standard method showed bursal involvement alone; in the remaining 10 patients every degree of bone destruction, from the slightest surface erosion to extensive cavitation, was observed.

Trochanteric tuberculosis probably spreads as a surface infection, although in a few cases the presence of large sequestrums suggests an infection in depth at the same time. In the patients with bone destruction the area of disease was well demarcated, and a uniform hard surface of bone presented after removal of the sequestrums and tuberculous debris. In view of this, excision of the trochanter appears to be superfluous and possibly dangerous, even in the presence of antibiotics. Roentgenography is an unreliable guide; decalcified sequestrums and debris are often not shown. Some useful information may be gained by roentgenograms in full medial and lateral rotation. In the absence of gross secondary infection the amount of discharge may be a rough but useful guide to the amount of dead tissue present. The results obtained from combined chemotherapy and radical surgery in the 18 patients treated by this method have been satisfactory so far, although the period of follow-up is still short. The results compare favorably with those of other methods of treatment employed in the group of 14 patients with trochanteric tuberculosis.

Gastrojejunal Ulcer and Gastrojejunocolic Fistula. R. P. McBurney, T. Farrar and R. L. Sanders. Am. Surgeon 24:709-713 (Oct.) 1958 [Baltimore].

Gastrojejunal ulcers developed in 51 of 1,000 patients treated surgically for duodenal ulcers. Five of the 51 had gastrojejunocolic fistulas. In 36 of the 51 patients a gastrojejunal ulcer developed after gastroenterostomy; 10 of these 36 had had vagotomy in addition to the gastroenterostomy. Nine patients had had gastric resection as their primary surgery, 5 had had vagotomy and gastric resection, and 1 had had a pyloric exclusion operation. The most common symptoms in this series were abdominal pain, nausea, vomiting, hemorrhage, weight loss, and diarrhea. Roentgenologic findings were positive or suggestive in 80% of the cases.

Fifty-eight surgical operations were performed on the 51 patients, since the gastrojejunal ulcer recurred in 7 of them. The majority of the patients were treated either by gastric resection with takedown of the gastroenterostomy, by vagotomy and gastroenterostomy combined, or by vagotomy plus gastric resection. There were 26 patients on whom gastric resection with resection of the stomal ulcer and performance of a new gastrojejunostomy were done. Seventeen of these obtained excellent and 5 satisfactory results, whereas in the other 4 patients the results were poor. In 12 patients vagotomy was added to gastroenterostomy in the treatment of gastrojejunal ulcer, with 2 excellent results and 10 poor results.

Nine patients had vagotomy and resection as their final definitive treatment, this being done as subsequent procedures in some cases. Of this group, 4 had excellent results; 1, a satisfactory result; and 4, unsatisfactory results. All these patients had had at least a 65% gastric resection in association with vagotomy. The primary causes for an unsatisfactory result in both the gastric resection cases and the vagotomy plus gastric resection cases were anemia and malnutrition plus the dumping syndrome. In only one case was recurrence of the ulcer the cause for an unsatisfactory result.

There were 2 postoperative deaths. Both of these patients had a gastrojejunocolic fistula, and one had a free perforation with peritonitis before operation. The authors believe that, with modern techniques and antibiotics, the treatment of choice for gastrojejunocolic fistula is a one-stage resection of the stomach, the ulcer, and closure of the colonic fistula. The last 3 of their 5 patients with gastrojejunocolic fistula all had uneventful postoperative courses. One of the patients had a pancreatic islet cell adenoma in association with a recurrent gastrojejunal ulcer. This was discovered at autopsy, the patient having died after hemorrhage caused by erosion of the splenic artery from a recurrent gastrojejunal ulcer. It is possible that some of the other patients in this series may have had this syndrome. The policy of the authors now is always to explore the pancreas when operating for gastrojejunal ulcer. Three patients had free perforation of the gastrojejunal ulcer into the abdominal cavity, and one of these had free perforation on 2 occasions. This complication was treated satisfactorily in 2 cases by simple closure of the perforation. In one case peritonitis led to abscess formation, and a second free perforation later was treated by radical resection; however, the patient died of peritonitis.

Adenomatous Polyps of the Duodenum. I. I. Kal'chenko. Novy. khir. arkh. 4:31-40 (July-Aug.) 1958 (In Russian) [Kiev, Russia].

On the basis of observations on 5 patients with polyps of the duodenum, the author concludes that most polyps of the duodenum are associated with polyposis of the stomach. The adenomatous polyps of the duodenum have the same tendency to undergo malignant degeneration as the polyps of the stomach, and they must, therefore, be regarded with suspicion. The adenomatous polyps of the duodenum, particularly if multiple and of considerable dimension, require resection of the intestine.

Removal of the polyps alone is not sufficient and is indicated only in cases in which the polyps are located near the papilla of Vateri, have not undergone malignant degeneration, and do not cause profuse hemorrhages. A thorough examination of the entire gastrointestinal tract is necessary in the presence of polyps of the duodenum, because they are frequently associated with polyps of other segments of the intestine. Clinical experience suggests that the polyps have a tendency to increase in number and in size and that they display a tendency to the involvement of other segments of the intestine.

GYNECOLOGY & OBSTETRICS

Femoral Neuropathy in Abdominopelvic Surgery. D. A. Johnson and R. R. Montgomery. M. Ann. District of Columbia 27:513-514, 562 (Oct.) 1958 [Washington, D. C.].

A case is reported which is a typical example of femoral neuropathy complicating gynecologic surgery. The 40-year-old woman was subjected to total hysterectomy, bilateral salpingo-oophorectomy, and appendectomy. The operation was performed through a Pfannenstiel incision. The immediate postoperative course was uneventful. On the third postoperative day, when the patient attempted to stand, her right leg did not support her. The patient remained in bed for a 4-day period and then attempted to stand and walk again. There was great weakness in the right lower extremity, particularly at the knee. The patient did not complain of pain in the extremity, but it was necessary for her to walk with a cane. Examination 6 weeks after the operation revealed weakness in the right lower extremity, with inability to extend the leg at the knee and to flex the thigh on the abdomen. The patellar reflex was absent; the Achilles tendon reflex was normal. There was deficiency of muscle tone over the anterior aspect of the right thigh, and measurements revealed approximately 2 in. of atrophy in the right thigh as compared with the left. A sensory deficit was detected over the anterior aspect of the right thigh.

A diagnosis of traumatic femoral neuropathy was made. The patient was reexamined 3 weeks later, when a very slight contraction in the right quadriceps muscle was palpable. One month later there was definite contraction of both the quadriceps and the iliopsoas muscles, though weakness was still severe and ambulation required support by a cane. Improvement continued slowly but progressively. The authors discuss the anatomy of the femoral nerve and suggest that some cases of femoral neuropathy may not be recognized. Often the complaint is one of vague weakness in one or both lower extremities which, fortunately, improves spontaneously in most instances in from 1 to 24 weeks. Symptoms vary according to the degree of involvement of the nerve. Weakness of flexion of the thigh at the hip and weakness of extension of the leg at the knee, with loss of the patellar reflex, are the prominent clinical features. If involvement is bilateral and severe, the patient may be unable to walk, and even standing may be very difficult. Retraction associated with surgery is the usual cause of this neuropathy. Awareness of the possibility of this complication may result in its prevention and will lead to its prompt recognition and appropriate treatment.

PEDIATRICS

The Heart in Funnel Chest: Preoperative and Postoperative Studies of 70 Cases. B. Landtman. Ann. paediat. Fenniae 4:181-190 (No. 3) 1958 [Helsinki].

Cardiologic studies were carried out on 70 children (50 boys and 20 girls) with funnel chest at the time of surgical correction of chest deformity. The children ranged in age from 9 months to 15 years, 45 being under 5 years. The interval between preoperative and postoperative examinations was, on the average, 4 or 5 months. Before the operation 22 of the children gave a history of repeated upper respiratory infections; 23, of dyspnea on effort; and 5, of occasional precordial pain. None of the patients showed signs of organic heart disease or of cardiac failure. The blood pressure was within normal limits in all the patients, and no significant changes were seen after the operation. Two of the children had systolic murmurs, the intensity of which exceeded normal ranges of variation; in both these patients the murmur almost disappeared after the operation. The rest of the patients showed normal phonocardiograms, and no significant changes were seen postoperatively.

Roentgenologic studies revealed in most of the patients slight enlargement of the cardiac silhouette and some degree of displacement to the left. The diameter of the heart was usually diminished in the lateral positions. After surgical correction of the chest deformity, the cardiothoracic ratio in the anteroposterior position decreased in two-thirds of the patients. Ectopic arrhythmias were recorded in 7 patients; normal sinus rhythm was restored in 5 of these patients after the operation. Postoperatively, the amplitude of the P wave decreased in 22 patients. Before the operation the majority of the patients showed electrocardiographic signs of clockwise rotation of the heart about its longitudinal axis. There was usually a positive correlation between the degree of the rotation and the severity of the sternal depression. A rotation of the heart in normal direction was usually seen after the operation. It was suggested that the preoperative changes in the electrocardiogram resulted from pressure exerted on the heart by the depressed sternum and from cardiac displacement. Although the majority of the children were asymptomatic before the operation, the observations tend to support the view that surgical correction of funnel chest is often indicated because changes in the function of the heart, which are often present in children with this anomaly, usually disappear after the operation.

Salmonella Typhimurium Infection Dust-Borne in a Children's Ward. J. G. Bate and U. James. Lancet 2:713-715 (Oct. 4) 1958 [London].

In an infants' ward of a children's hospital 7 outbreaks of gastroenteritis over a period of 11 months were caused by Salmonella typhimurium, phage type 2. The Sal. typhimurium infection was probably introduced in November, 1956, by a child who had had gastroenteritis in another hospital and who was found to be an intermittent excreter. Even at this early stage there was evidence of an environmental infection in the finding of these organisms in the weighing-machine basket. On investigation of the second and third outbreaks, a nurse, 2 orderlies, and 2 porters were found to be excreters. It seemed highly probable that the porters had been infected by handling contaminated linen. In the last 4 outbreaks no human carrier was detected, and it was not possible that the infection had come from the milk-kitchen. Therefore, there was reason to believe that the infection was environmental. This was confirmed by the finding of Sal. typhimurium, phage type 2, in the bag of the floor-polisher. It seemed likely that dust contamination by passage of organisms through the porous cloth bag of this machine was the cause of the later outbreaks, and may have been responsible for all but the first. Since suction-cleaning and polishing of floors by a machine fitted with disposable paper dust-bags has been substituted, there has been no case of Sal. typhimurium infection.

Plasmanate: A New Plasma Substitute for Pediatric Therapy. T. C. Cock, C. M. Binger and J. L. Dennis. California Med. 89:257-259 (Oct.) 1958 [San Francisco].

The authors report the results of a 2-year study on 125 infants and children who received intravenous infusions of a fractionated human serum protein solution, Plasmanate. More than 300 units of the solution were given during this period. The response to this new plasma substitute was studied in detail in 120 of the 125 patients, 94 of whom were in extreme shock state associated with the dehydration of diarrhea, toxemia, and infections and with extensive burns; the remaining 26 were chronically ill children who had pronounced serum protein deficiencies due to such causes as idiopathic hypoproteinemia, malnutrition, and burns. All the children were observed for any reactions, complications, or problems that might be associated with the infusion of human serum proteins. The group of children who were in extreme shock state were given 30 cc. of Plasmanate per kilogram (15 cc. per pound) of body weight intravenously at 5 to 10 cc. per minute. Children with hypoproteinemia were given daily slow intravenous drip infusions of 20 to 30 cc. per kilogram (10 to 15 cc. per pound) of body weight, as required. There was rapid response to stimuli, improved orientation, and restoration of normotensive blood pressure in 89 of the 94 patients who were in acute shock state; 22 of the 26 children with persistent hypoproteinemia responded with return of strength, gain in weight, and satisfactory healing of surgical incisions and skin grafts. Eleven had a significant increase in serum protein content after repeated administration of Plasmanate. In no instance was there any evidence of sensitization, untoward reaction, or hepatitis, although 29 patients received repeated infusions at varying intervals. The authors believe that Plasmanate, which has relatively more sodium (111 mEq. per liter) than chloride (61 mEq. per liter), osmotic pressure parallel to that of plasma, acidity within physiological limits, and negligible potassium content, would constitute an almost ideal solution for initial therapy in infants with acidosis, dehydration, and electrolyte depletion.

Behavior of Antistreptolysin Titer After Recovery from Scarlet Fever. H. Kupatz and W. Köhler. Monatsschr. Kinderh. 106:393-396 (Sept.) 1958 (In German) [Berlin].

From earlier investigations on the behavior of the antistreptolysin titer during scarlet fever, the authors had deduced that contact with hemolytic streptococci must persist for a while before an increase in antistreptolysin titer can be expected. Observations on the streptolysin titer after recovery from scarlet fever proved somewhat confusing, for, if the hemolytic streptococci had been rendered inactive by penicillin, no increase in the titer should have been evident 3 weeks after discharge from the hospital in those who had had normal titers at the time of admittance. The contrary was observed in that there was an increase in antistreptolysin titer in 11 of 17 children. Other investigators likewise had observed late increases in titers despite penicillin therapy. Since opinions were divided about the causes of this behavior, the authors investigated this problem in a larger number of patients. Pharyngeal smears were taken to demonstrate the presence of hemolytic streptococci.

Studies were made on 162 children, but it was not possible to subject all these children to follow-up tests at regular intervals. At the time of discharge from the hospital only 21% of the children showed an increased antistreptolysin titer, whereas during follow-up tests an average of 57% showed increases. The increase became even more clear when the results obtained within the first 5 weeks (50%) were compared with those obtained in later weeks (70%). It was ascertained by questioning that these increases were not brought on by new infections. The fact that an increase in antistreptolysin titer developed in more than half of the cases of scarlet fever proved that, despite early treatment with penicillin, the patients reacted to the presence of hemolytic streptococci more often than was generally assumed. Although it was impossible to isolate hemolytic streptococci from the pharyngeal smears after penicillin therapy had been continued for 7 days, control tests carried out from 3 to 8 weeks after discharge from the hospital, and even later, revealed hemolytic streptococci in the pharynx of about 29% of the patients examined. When patients were divided into 2 groups with regard to an increased or normal antistreptolysin titer, the percentages were 47 and 7% respectively.

No definite answer can be given to the question whether the hemolytic streptococci found during follow-up tests were acquired as the result of a superinfection or were identical with the streptococci which produced the scarlet fever. The strains of hemolytic streptococci were classified serologically. The large majority of strains belonged to Streptococcus pyogenes humanus, group A. Six strains, however, belonged to other groups. Of 4 of these which were isolated on admission, 2 belonged to group F, 1 to group C, and 1 to group P. This was the first time that a Streptococcus organism of the serologic group P was demonstrated by the authors in a human subject; usually it is detected in dogs or hogs. The child in question had typical scarlet fever and had lived in rural surroundings.

Etiology of the Stevens-Johnson Syndrome. G. Bucha. Monatsschr. Kinderh. 106:401-404 (Sept.) 1958 (In German) [Berlin].

According to Bucha, the severe forms of erythema exudativum multiforme show an extraordinary variety of manifestations. This is explained by the involvement of the different mucous membranes and of internal organs. Many factors have been listed as eliciting causes, and even the nomenclature is not uniform. The idiopathic form, ectodermosis erosiva pluriorificialis, is generally referred to as the Stevens-Johnson syndrome. The 3 most frequently suggested etiologies of this syndrome are (1) that it is an independent virus disease, (2) that it is a form of sepsis, and (3) that it is an allergic-toxic process which probably belongs to the group of rheumatic disorders. Even the therapeutic results are often contradictory, so that a diagnosis *ex juvantibus* is likewise not possible.

The author resumes an earlier discussion on this disorder, because he was forced to reconsider some views he had expressed about 3 previously presented cases. In 2 of these patients, who at first were considered as having an independent disease entity, that is, a form of sepsis, there occurred after more than a year similar symptoms. The author has now changed his view on the etiology in that he no longer considers this as an idiopathic form of the Stevens-Johnson syndrome but rather as a symptomatic form. He believes that the process was elicited by an infection with cocci, such as are frequently found in infections of the nasopharynx. These catarrhal manifestations apparently do not represent the prodromal stage of the Stevens-Johnson syndrome but represent a particularly severe form of an allergic reaction to various organisms.

The third patient, who had had articular lesions, glomerular nephritis, and endocarditis and in whom the antistreptolysin titer had been very high, is now considered as having had a process in which these manifestations were not the accompanying symptoms of the Stevens-Johnson syndrome but rather were symptoms of a rheumatic process. It is assumed that even the apparently idiopathic forms of the Stevens-Johnson syndrome are immunobiological manifestations which can be elicited by various micro-organisms, particularly streptococci. The therapy should always employ antibiotics, but the administration of adrenocortical preparations has been found to be an effective adjuvant to the antibiotic therapy.

Disseminated Lipogranulomatosis (Farber's Disease). R. Zetterström. Acta pædiat. 47:501-510 (Sept.) 1958 (In English) [Uppsala, Sweden].

The author reports on a 4-month-old boy, admitted to the pediatric clinic of Karolinska Sjukhuset in Stockholm, who presented symptoms which resembled those of rheumatic arthritis and which appeared to be identical with those described by Farber at the congress held by the American Pediatric Society in 1952. The boy was the second child of healthy unrelated parents. No heredity for any special disease could be found, and the older sibling was healthy. In the patient intense vomiting of the type associated with stenosis of the air passages (high-level obstruction) was observed during the postnatal period, as well as persisting hoarseness, but otherwise no specific abnormalities could be detected. Examination at the age of 4 months revealed an irritable infant, weighing 4,640 Gm. (10¼ lb.). The tissues were somewhat loose, the face was unusually puffy, the tongue was somewhat large, the hand joints were swollen, and the fingers were in flexion contracture. There was marked spindle-shaped swelling of the periarticular tissues around the interphalangeal joints, and the knee joints were swollen. The liver was slightly enlarged. The diagnosis was generalized moderate lymphadenopathy.

Despite treatment with cortisone in high doses (40 mg. daily), periarticular joint changes, with involvement of the periarticular tissues, progressed in this patient. The only effect of cortisone treatment was that the pain was thought to decrease. All joints, with the exception of the shoulders, slowly became affected with redness and swelling. At the age of 10 months subcutaneous granulomas appeared on the scalp and over the ribs, hoarseness increased, and the patient gained very little weight. At the age of 15 months he was dystrophic, with poorly developed musculature and sparse subcutaneous fat, and aphonic, with significant respiratory difficulty. In addition to the periarticular changes, numerous bean-sized, subcutaneous, easily movable, moderately firm granulomas had developed over both large and small joints. These granulomas consisted histologically of so-called foam cells. Laryngoscopic examination showed narrowing of the air passages due to granuloma formation. Tracheotomy was performed. A xanthoma-like growth, about the size of a rice kernel, in the conjunctiva of the left eye was excised.

The boy was cared for at the clinic for a total of 11 months, after which at the age of 26 months he was transferred to another hospital; during this time the disease progressed slowly. The examinations which were carried out have given no information as to the etiology and pathogenesis of the disease. No definite metabolic disturbances typical for this disease could be demonstrated in vivo. However, nothing speaks against Farber's hypothesis that the disease is caused by a disturbance in lipid metabolism.

DERMATOLOGY

The Use of Impatiens Biflora (Jewelweed) in the Treatment of Rhus Dermatitis. R. A. Lipton. Ann. Allergy 16:526-527 (Sept.-Oct.) 1958 [St. Paul].

The fresh juice of jewelweed (Impatiens biflora) is reputed to be efficacious in the treatment of rhus poisoning. The substance is a tincture made by maceration of I. biflora, representing 10% dry drug strength and containing 54% alcohol. The mechanism concerned in the action of this drug in the case of rhus dermatitis is not definitely established. When the author used this agent in cases of rhus dermatitis, he diluted 1 part of the standard preparation with 4 parts of water and used the diluted mixture as a topical application on the affected skin. The present study deals with 115 patients afflicted with rhus dermatitis whom he treated during the past 15 years. All had the acute stage of rhus dermatitis and were seen shortly after their exposure to the weeds and the appearance of the skin eruption.

Some patients were treated with jewelweed alone, and others were treated partly with jewelweed and partly with other medications. Thirty of the 115 patients had certain portions of the affected skin treated with a mixture of calamine lotion and 0.1% menthol, and the rest of the lesions treated with the jewelweed preparation. Another group of 30 patients was treated partly with Burow's solution, in dilution 1:20, and partly with jewelweed. A third group of 6 patients was treated with a 0.5% hydrocortisone ointment applied locally to some portions of the involved skin and jewelweed applied to other parts. From observations on these patients and from experiments on himself, the author concludes that jewelweed is a potent and safe therapeutic agent in the treatment of rhus dermatitis. He regards jewelweed as an excellent substitute for corticotropin (ACTH) and the corticosteroids in the treatment of poison ivy dermatitis. The topical application of corticosteroids has been disappointing, partly because the oily nature of the vehicle may cause spreading of the lesion rather than arresting it.

Oral Manifestation in Lichen Ruber. G. Ranstrup and J. J. Pindborg. Ugesk. læger 120:1327-1330 (Oct. 2) 1958 (In Danish) [Copenhagen].

Lichen ruber at some time in its course is often accompanied by characteristic affections in the oral cavity, and it can occur localized exclusively to the mouth cavity. There were, or had been, cutaneous manifestations of lichen ruber in 5 of 15 patients with lichen ruber in the oral cavity. The histological features were typical of the disorder. In 2 patients control about a year after the first examination showed that the eruption in the mouth had disappeared. It is important to distinguish between lichen ruber and leukoplakia, as the latter is a precancerous condition.

OPHTHALMOLOGY

Polyarteritis Nodosa with Ophthalmic and Neurological Complications. B. Sheehan, D. G. F. Harriman and J. P. P. Bradshaw. A. M. A. Arch. Ophth. 60:537-547 (Oct.) 1958 [Chicago].

The authors report on a woman with polyarteritis nodosa, who was 30 years old at the onset of the disease. At the age of 33 years, eye symptoms commenced, first as teichopsia and within 3 weeks as defective vision in the right eye. There was a small area of perivasculitis of the retina around the macula of the right eye, and near it there were 2 or 3 small white exudates no larger than miliary tubercles of choroid. There was at that time no edema of the retina or of the optic disk. In the course of the next 5 months the acuity of the right eye gradually became less than the ability to count fingers. Keratic precipitates occurred in it, remaining constantly thereafter, and there were also striking changes in the fundus; these consisted of multiple retinal hemorrhages, massed white exudates around the macula, retinal edema and papilledema, and a considerable amount of raised white exudate inferiorly projecting 10 D. By contrast, the appearance of the left eye remained entirely normal throughout the illness. After a short quiet period the changes in the right eye became more acute; fresh keratic precipitates were deposited, and small vitreous hemorrhages occurred. The vitreous then cleared, revealing the gross fundus changes still spreading. On 2 occasions the patient complained of intense pain in the eye during the night, and, in view of the possibility of a secondary glaucoma, the eye was enucleated.

Various neurological syndromes also developed, including sensory neuropathy of the trigeminus, lumbar radiculopathy, polyneuritis, epilepsy, and a confusional psychopathy, terminating in coma. Furthermore, there occurred intestinal obstruction due to a diffuse abnormal condition of the ileum and colon. Extensive studies were made, and they were for the most part negative, though the erythrocyte sedimentation rate was persistently increased. During the terminal stages of her illness the patient had intermittent fever, leukocytosis, and inversion of the albumin-globulin ratio and failed to improve when she was given antibiotics or cortisone. She died at the age of 35 years. The general postmortem findings indicated some indeterminate form of disseminated vascular disease, but the histopathological study of the enucleated eye revealed polyarteritis nodosa of the retinal vessels and thus showed that the basic condition was, in fact, active polyarteritis.

Treatment of Recurrent Styes. P. W. M. Copeman. Lancet. 2:728-729 (Oct. 4) 1958 [London].

The author defines a stye as a furuncle of the eyelash follicle, caused by Staphylococcus aureus. The sporadic type appearing as an isolated incident is a self-limiting condition of minor importance, but recurrent styes present a different problem. The styes may be so severe and frequent that the patient is partially disabled, though in every other respect he may be healthy. This condition is often refractory to treatment. The potential danger is illustrated by 2 patients who were admitted to St. Thomas's Hospital, London, in 1957 with cavernous sinus thrombosis after a stye. One of these died. The subjects of the investigations described were patients who presented with a stye; they had previously had at least one stye within the preceding month, and many had a continuous succession without any break. Cotton-wool swabs soaked in sterile broth were used to collect samples from each of the anterior nares and from the eyelid margins of both eyes at every attendance of the patient. Thirty-six patients with recurrent styes were examined, and from 34 of these Staph. aureus was isolated on one or more occasions. This is a far higher figure than that found among the general population and among those who have styes sporadically.

Patients received treatment to the anterior nares alone and none locally to the eyelids. Alternate patients were treated with the antibiotic ointment and with the inert base. The antibacterial ointment used was a neomycin-gramicidin mixture, Graneodin. Both these antibiotic ingredients are effective against the Staphylococcus organism. All patients were given an explanation of the rationale of the treatment, until their cooperation had been obtained. A small amount of ointment was placed into each vestibule of the nose with a matchstick and spread by inunction with the little finger. The initial application of the ointment was 4 times a day for 10 days. The run of styes was broken by eliminating Staph. aureus from the anterior nares with the aid of Graneodin. Although treatment of the nares alone is generally sufficient, it is logical to treat the stye itself also to avoid transference of infection. Therefore, it is recommended that the most satisfactory treatment for recurrent styes involves simultaneous application of "nonsystemic" antibiotics to both eyelids and to the anterior nares.

PATHOLOGY

Asian Influenza: A Study of 150 Persons During the 1957 Pandemic. D. P. Buebendorf, T. E. Carson, N. R. Cooper and others. Yale J. Biol. & Med. 31: 14-28 (Sept.) 1958 [New Haven, Conn.].

Of 150 persons selected and studied by the authors for a 3-month period, which included the entire duration of the type A Asian influenza epidemic in the fall of 1957, the first group of 50 were volunteers from the Yale Medical Center, between the ages of 18 and 36 years, to whom 2 injections of commercially prepared, monovalent Asian strain vaccine had been given before the epidemic. The second group of 50 persons was composed of unvaccinated volunteers chosen from the same community as those of the first group and comparable with the latter as to residence, contacts, and age. The third group of 50 persons were chosen from unvaccinated persons who were institutionalized at a training school for the mentally retarded. Paired serums from each participant in the study were analyzed by both the complement-fixation and the hemagglutination-inhibition technique, but no attempt was made to isolate influenza virus.

The serologically confirmed clinical attack rates for the 3 groups were as follows: one out of 50 for the vaccinated group, 16 out of 50 for the comparable unvaccinated group, and 28 out of 50 for the institutionalized unvaccinated group. Significant antibody rises occurred in 27 of the 50 persons in the vaccinated group, presumably due to the effect of the vaccine. In the comparable unvaccinated group, presumed subclinical infections occurred in 9 persons, and in 11 persons in the third group. The combined subclinical and verified clinical cases gave an attack rate of 50% for the group of unvaccinated persons from the Yale Medical Center and an attack rate of 78% for the institutionalized group. There was no occurrence of antibody rise in 11 of the 56 reported clinical cases.

Differences were observed in the results of the complement-fixation and hemagglutination-inhibition tests. Some persons showed increased titers in both serologic tests, a few had an antibody rise by hemagglutination inhibition only, and many showed a response by complement fixation only. Ancillary tests performed on the serums which showed an antibody rise by complement fixation only excluded as responsible factors either an egg contaminant in the vaccine or a cross reaction with another type A or A′ Asian influenza virus. The serologic results indicated that neither the hemagglutination-inhibition nor the complement-fixation test alone was sufficient for the serologic diagnosis of Asian influenza, and that diagnosis was more often made when both of the tests were used together.

After the conclusion of the formal study another influenza-like epidemic struck the Yale Medical Center community in January and February, 1958. Twenty-five persons in the original vaccinated group reported influenza-like illnesses during this "second wave," and 13 of these had shown a serologic response during the original study. Fourteen persons in the original unvaccinated group reported influenza-like illnesses during this second epidemic, and 5 of these had had serologic evidence of influenza during the first epidemic.

Papillary Cancer of the Thyroid: A Review of 25 Years of Experience. E. L. Frazell and F. W. Foote Jr. Cancer 11:895-922 (Sept.-Oct.) 1958 [Philadelphia].

The authors show that much confusion persists concerning almost all aspects of papillary adenocarcinoma. The fact that no single observer or group has had sufficient experience with all manifestations of this form of cancer emphasizes the need for extreme caution in making all-inclusive pronouncements of a prognostic nature about a form of cancer in which the most noteworthy attribute is extreme chronicity. The authors review the experience of a single surgical service in the diagnosis and treatment of papillary adenocarcinoma of the thyroid during the 25-year period from 1930 through 1954. The diagnosis of carcinoma of the thyroid was confirmed in 725 patients seen on the head and neck service of Memorial Center for Cancer and Allied Diseases in New York. All histological material was reviewed, and, on the basis of generally accepted standards, 393 (54.2%) of the tumors were classified as papillary. This study includes all patients observed by the authors —those with early or advanced cancer, those treated first at Memorial Hospital, and those referred to this hospital after being treated elsewhere (whether or not they were treated at this hospital after referral). Clinic "shoppers" and patients lost to follow-up after treatment are also included. This experience with papillary thyroid cancer differs considerably from that reported by other observers, since it is the experience of a specialized surgical service within an institution largely devoted to the diagnosis and treatment of cancer. The differences observed confirm the fact that, when seen in sufficient numbers, the group of thyroid cancers usually designated as papillary may exhibit considerable variation in pathological appearance and clinical course.

There were frequent deviations from the traditional concept that papillary cancers of the thyroid are usually found as firm, solitary, and asymptomatic thyroid nodules in comely young female patients with or without regional adenopathy. Unusual manifestations of local, regional, and distant spread were encountered in all age groups, in both sexes, and in the patients being treated for the first time as well as those previously treated. Such findings were frequent enough to serve as a warning against the apparently growing belief in the essentially benign nature of these tumors. The sluggish nature of this disease makes the conventional 5-year follow-up studies inadequate to determine its true lethal properties and its response to different methods of treatment. Long-term observations were hampered by limited material, but some evidence was accumulated to suggest that long-standing tumors may be expected to accelerate their invasive properties after years or decades of relative quiescence.

This experience fails to settle the issue of whether routine neck dissection for metastatic papillary cancer will be the deciding factor in the ultimate survival of the patient, but evidence is presented that systematic removal of such metastatic nodes is a step in the right direction. It is evident that dogmatic statements concerning the superiority of one treatment over another are unwarranted at this time. Lacking convincing evidence to the contrary, it seems logical to believe that metastatic nodes from papillary thyroid cancer are way stations in the dissemination of the disease and that their elimination should be an integral part of the initial treatment.

Carcinoma of Sweat Gland Origin: Report of a Case of 30 Years' Duration with Autopsy Findings. J. J. Moran and R. C. Horn Jr. Surgery 44:683-688 (Oct.) 1958 [St. Louis].

The authors report an unusual case of malignant papillary cystadenoma of sweat gland origin in a man who was 31 years old when he was admitted to the Hospital of the University of Pennsylvania, in Philadelphia, for a painless, slowly growing mass on the radial aspect of the left wrist, about 4 cm. proximal to the radial styloid process. The lesion had first been noted after an accident in which a steel sled runner had passed over the wrist, without, however, producing a serious injury in the patient who at the time was 16 years old. Two attempts at excision, when the patient was 26 and 29 years old, were followed by local recurrence. On admission to the university hospital a third excision was attempted, but the tumor was too extensive to permit complete removal. An epitrochlear lymph node was removed and found to contain tumor tissue. A definite diagnosis of malignancy was made, and amputation was advised but refused. Nineteen months later the arm and hand had become markedly edematous, and many nodules were palpable in the scarred area on the radial aspect of the forearm. Amputation was performed just distal to the deltoid insertion, but above the upper limits of the edema. Examination of the amputated arm revealed a large tumor invading and destroying all the soft tissues of the dorsal part of the distal 12 cm. of the forearm.

The patient remained symptom free for 3 years. Then low-back pain developed, which radiated along the medial aspect of the toes of the left leg accompanied by paresthesias along the outer aspect of the right thigh. A roentgenogram revealed a destructive lesion of the 5th lumbar vertebra, which was treated by irradiation therapy. In the following years tumor nodules were excised repeatedly from the left shoulder region, and irradiation therapy was given to this region postoperatively. Metastases formed in the lungs, and the patient died shortly after his 12th admission to the hospital, 15 years after the definite diagnosis of malignancy had been made. All the surgical specimens removed at the university hospital were characterized by cystic structures lined by orderly cuboidal epithelium, with varying sized intraluminal papillary epithelial proliferations. This histological pattern was still apparent throughout the widespread metastases found at autopsy. Multiple tumor nodules were present in the skin of the left side of the chest, both pleural cavities, the epicardium, and the lungs; thoracolumbar spine, pelvis, and many ribs were other sites of metastasis. The mediastinal, retroperitoneal, and pelvic lymph nodes were converted into huge, matted tumors. The tumors, as seen in the autopsy material, differed from the surgical specimens only in a lesser tendency toward cyst formation and papillary pattern and a slightly greater tendency toward growth in solid masses. The over-all known duration of the neoplasm was 30 years. Throughout this period the tumor maintained an orderly intracystic papillary pattern. The tendency of carcinoma of sweat gland origin to be well differentiated and to grow slowly makes it a particularly insidious type of neoplasm.

Tissue Chrysophoresis. O. C. Croxato. Medicina 18:8-11 (Feb.) 1958 (In Spanish) [Buenos Aires].

"Tissue chrysophoresis" is a term used to designate the diffusion of gold after gold therapy to the various organs of the body. The author found in previous work that gold was identified in various organs during autopsies on persons who had been treated with gold preparations and who had died of chronic pulmonary tuberculosis. Gold in histological specimens manifests itself in the form of minute yellow "refringent granules" of uniform size, which occupy the cytoplasm of the macrophages and the polynuclear cells or are found in a free form in the intercellular substance of the connective tissue. The particles of gold are clearly visible in commonly stained histological specimens whenever the microscopic condenser is lowered and the diaphragm is semiclosed. The number of gold granules in specimens from the bodies of persons who during life had chrysocyanosis is very large.

In the department of pathological anatomy of the Hospital Muñiz of Buenos Aires, autopsies were made on 12 persons who had received gold therapy and who had died of chronic pulmonary tuberculosis. The ages of the patients ranged from 17 to 57 years. The gold preparations given to the patients varied in dosage between 0.32 and 12 Gm. The time which elapsed between discontinuation of gold treatment and death ranged from 1 month to 8 years. Observations on lungs and brains at autopsy are not reported, but gold was found in all the organs in more or less large amounts. The myocardium and the liver had the greatest amount in all cases. The author also performed experiments on rabbits and guinea pigs which received gold preparations for some time before being killed for histological study of their organs. Histochemical researches were carried out on nonstained histological specimens, the reducing agents being tin chloride and hydrochloric acid (Christeller's modified technique). They gave positive results for gold in both autopsy material and that from experimental animals.

The author concludes that gold is the only metal which travels in the human body by way of the macrophages and the polynuclear cells. Retention of gold in a given organ injures the tissues of that organ. The degree of retention of migratory gold in a given organ has no relation to the dose of gold administered to the patient and the time which has passed between the last injection of the metal and the occurrence of death; it depends on individual predisposition. The author directs attention to the fact that no previous report on tissue chrysophoresis after gold therapy has been reported in the literature. Further studies on tissue chrysophoresis will improve our knowledge about the system of macrophages, and they will clarify certain immunological problems concerning the persistence of antigens in the body.

BOOK REVIEWS

Clinical Radiology of Acute Abdominal Disorders. By Bernard S. Epstein, M.D., Associate Clinical Professor of Radiology, Albert Einstein College of Medicine, Yeshiva University, New York. Cloth. $15. Pp. 352, with 406 illustrations. Lea & Febiger, 600 S. Washington Sq., Philadelphia 6, 1958.

This work represents an attempt at "concisely correlating the radiologic manifestations of the 'acute abdomen' with clinical and pathological processes." As the author states, it is difficult to define the acute abdomen and equally difficult to limit any treatise to the acute emergencies alone. Epstein has adequately discussed and amply illustrated 104 separate topics which comprise those conditions which, while not "dramatic and catastrophic" in nature, still are intense and may require medical attention. This book deals chiefly with the gastrointestinal tract, but also includes examples of or references to the other organs whose malfunctions make up the clinical picture of the acute abdomen. About the report on radiologic examination the author states: "There is no such thing as a 'routine' and the most dangerous study is the one reported as 'normal.'" Most of the illustrations are of typical cases of common diseases, collected chiefly from the author's personal experiences. The legends are simple, to the point, and not cluttered with numbers or letters. Usually each figure has one focal point of interest and this is either clearly demonstrated or identified by arrows. The text has been kept to a minimum, but an adequate bibliography is added at the end of each section. The bulk of the text and illustrations have to do with the gastrointestinal tract and the illustrations for the most part are from examinations done with barium or some other contrast medium. The author discusses the commonplace as well as some of the less common conditions such as ulcerogenic pancreatic adenoma, cast syndrome, and blood dyscrasias.

One of the best features is the high quality of the photographic reproductions of the roentgenograms. Often there are either several views of the lesion in question, multiple examples of the disease under consideration, or follow-up films on particular lesions. The most advantageous method of examination has been exploited in illustrating each condition, i. e., pneumoperitoneum with transabdominal views to outline adhesions or to demonstrate peritoneal metastatic nodules. The book does not deal chiefly with the scout (or plain) film of the abdomen or with the surgical abdomen, but rather with the roentgenographic manifestations of the diseases in question. It discusses the pathological changes (in some instances with direct photographic correlation with the gross specimens) and includes the pertinent symptoms. It does not deal exhaustively with genitourinary lesions such as salpingitis, ectopic pregnancy, genital tumors and their complications, renal infection, or renal lithiasis. Chapter 1 covers congenital disorders; chapter 2, neoplastic disease; chapter 3, inflammatory disorders, parasitic and granulomatous diseases, collagen disturbances, metabolic disturbances, and vascular disorders; chapter 4, traumatic disorders, foreign bodies, and effects of drugs. This book should appeal to gastroenterologists, internists, and radiologists.

Handbuch der Tuberkulose. In fünf Bänden. Herausgegeben von Prof. Dr. J. Hein, Direktor des Krankenhauses Tönsheide/Holstein, Prof. Dr. Dr. h.c. H. Kleinschmidt, und Prof. Dr. E. Uehlinger, Direktor des Pathologischen Instituts der Universität Zürich. Band I: Allgemeine Grundlagen. Bearbeitet von H. Bloch et al. Cloth. 178 marks; $42.40. Pp. 832, with 244 illustrations. Georg Thieme Verlag, Herdweg 63, (14a) Stuttgart, West Germany; Intercontinental Medical Book Corporation, 381 Fourth Ave., New York, 16, 1958.

This is the first of a series of five reference volumes on tuberculosis edited by a clinician, a pediatrician, and a pathologist. Volume 2 will cover clinical aspects of pulmonary tuberculosis, stressing recent experimental methods; volume 3, modern thoracic surgery (a revised edition of Hein, Kremer, and Schmidt); volume 4, extrapulmonary tuberculosis; and volume 5, social and economic aspects of the disease, including education, prevention, vaccination, and rehabilitation. The editors state justifiably that there is a need for an up-to-date reevaluation of the clinical and experimental knowledge of tuberculosis since the era of antibiotics and thoracic surgery has changed our original concepts of the pathology, course of disease, and epidemiology. These volumes will be a critical analysis rather than merely a compilation of the literature. It is stressed that tuberculosis is still a major disease and is far from being eradicated.

With one exception, the contributors to this first volume are of German (or Swiss-German) origin, and, with the proverbial German thoroughness, the following subjects are considered *in extenso:* the history of tuberculosis, biology of the tubercle bacillus, experimental immunobiology of tuberculosis, morphology of tuberculous allergy, tuberculosis and allergy, immunobiology, tuberculin and tuberculin sensitivity, the serum diagnosis of tuberculosis, epidemiology and statistical analyses of tuberculosis, sources of tuberculous infection and

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These book reviews have been prepared by competent authorities but do not represent the opinions of any medical or other organization unless specifically so stated.

methods of spread, internal and external factors influencing the course of the disease, and comparison of the pathology of tuberculosis in animal and man. These subjects are covered by 14 contributors. Their aim, to present most of the important published data and to slant the criticism toward future experimentation and treatment of the disease, has been accomplished. For example, almost 150 pages written by four authors are devoted to allergy and immunity in tuberculosis. It would appear from these discussions that the final separation of allergy from immunity is far from being established. In fact Schmid, of Heidelberg, believes that biologically, allergy activates the mesenchyme, mobilizes a more rapid and efficient phagocytosis, facilitates more tubercle formation, and promotes cytolysis. Thus we are back on the seesaw.

The chapter on tuberculin and tuberculin sensitivity by Kleinschmidt is timely since he discusses among other things the specificity of the larger doses of tuberculin. From his vast experience he concludes that 100 toxic units (0.1 ml. of 1:1,000 dilution of OT or 0.0002 mg. of purified protein derivative) is necessary to exclude a tuberculous infection. In 2 to 6%, 1,000 toxic units are needed to exclude known infection with tubercle bacillus. This evidence is contrary to what recently has been appearing in the American literature. Almost 250 pages are devoted to intrinsic and extrinsic factors that help determine the development and the course of a tuberculous implantation in animal or man. Many of these factors may influence the method of treatment. The epidemiology of tuberculosis is traced minutely from prehistoric times to the present with numerous tables and graphs. This book covers the topics mentioned in great detail. It should be considered as a reference book and should be made available to all interested in tuberculosis. The style is heavy, as is usual for reference books, particularly German ones. The exceptions are those chapters written by naturalized Americans (Suter and Bloch).

Transportation of the Injured: Emergency Procedures for Ambulance Crews, Training, Equipment, Vehicles, and Responsibility for Ambulance Service. By Carl B. Young Jr., M.P.H. Carl B. Young, M.D., F.A.C.S., collaborating physician. Cloth. $6.75. Pp. 238, with illustrations, drawings by Richard Fry Jr., B.S. Charles C Thomas, Publisher, 301-327 E. Lawrence Ave., Springfield, Ill.; Blackwell Scientific Publications, Ltd., 24-25 Broad St., Oxford, England; Ryerson Press, 299 Queen St., W., Toronto 2B, Canada, 1958.

The material in this monograph is presented in a concise manner with use of on-the-scene photographs of various accidents, cartoon illustrations, and diagrams of certain first-aid procedures which are appropriate for administration at the scene of an accident. Section 1 was prepared for the use of ambulance crews, law enforcement and fire service personnel, industrial nurses, and others responsible for the handling of the injured. Section 2 was written for the administrative heads of city governments, city and county police and fire departments, health units, hospitals, undertakers, ambulance service companies, county medical societies, and community leaders. Because first aid at the scene of an accident is often rendered by laymen, many physicians concerned with the treatment of injured patients, as well as the National Safety Council, have become concerned with the quality of such care and the care of the injured after they reach a hospital emergency service. The quality of emergency care at the scene of accidents should be improved and an organized effort in this direction might be made by local medical societies.

Section 1 covers general considerations in emergency first aid, including procedures at the scene of accident, identification, care for patients in shock, care of assault wounds, acute respiratory emergencies and resuscitation, the care of burned patients, emergency splinting of fractures, common medical emergencies, care for emergency births, care of mentally disturbed patients, and proper procedures in handling the dead. Section 2 covers training requirements for ambulance personnel, basic equipment for the emergency ambulance, records, and statistics. This manual is of a convenient size, readable in content, attractive as to format, and profusely illustrated. The procedures outlined in general follow standard accepted procedures for various acute injuries and emergencies such as prolonged immersion. The monograph should be useful as a text in conjunction with a program of instruction for first-aid workers.

The Neurologic Examination: Incorporating the Fundamentals of Neuroanatomy and Neurophysiology. By Russell N. DeJong, M.D., Professor of Neurology and Chairman of Department of Neurology, University of Michigan Medical School, Ann Arbor. Second edition. Cloth. $20. Pp. 1078, with 368 illustrations. Paul B. Hoeber, Inc. (medical book department of Harper & Brothers), 49 E. 33rd St., New York 16, 1958.

This volume retains all of the features of the first edition, published eight years ago, and there have been only minor changes. The writing is lucid and the chapters are well organized. Illustrations are ample, appropriate, and clear. References have been selected with care and are up to date. The author has generally succeeded in describing clinical neurological abnormalities in essential detail. This is not a textbook of neurophysiology or neuroanatomy, but sufficient information is provided to assist in both the interpretation of signs and understanding of modern theories of abnormal function. The author treats poorly understood phenomena with commendable caution and handles difficult topics like aphasia in comprehensible fashion. The author of any book centered about the neurological examination is bound to be criticized for including too much or too little, according to the reader's tastes and interests. There are physiological omissions, such as the role of the small motor nerve system in muscle tone, and relative neglect of current concepts of the neural basis of consciousness. There are also uneven features in the discussion of ancillary diagnostic methods; for instance, there are detailed chapters on spinal fluid and electrical stimulation of muscles but nothing on the various roentgenographic techniques or electroencephalography and little on electromyography or biochemical studies of blood and urine. Although not intended to be a textbook of neurology, problems of differential diagnosis are discussed in relation to particular aspects of the neurological examination. In addition, there are special sections on low back pain, vascular syndromes, states of disordered consciousness, and hysteria. The very excellence of this book paradoxically creates its major drawbacks. It is long and relatively expensive. These features make it unsuitable as a general textbook for medical students, although it should be an important reference for all students and practitioners. For those professionally involved in any of the neurological specialties it should continue to be a standard source of information.

Tumors and Tumorous Conditions of the Bones and Joints. By Henry L. Jaffe, M.D., Director of Laboratories and Pathologist, Hospital for Joint Diseases, New York. Cloth. $18.50. Pp. 629, with 701 illustrations. Lea & Febiger, 600 S. Washington Sq., Philadelphia 6, 1958.

Dr. Jaffe, one of the more eminent contributors to the literature of the pathology of bones and bone tumors, has gathered together his personal experience in this elegantly produced book. The presentation includes an adequate discussion of the clinical features and course, an excellent differential diagnosis, and a section on the radiologic and pathological findings of the conditions discussed. The radiologic appearances and the gross lesions are frequently juxtaposed in such a fashion as to be of maximal teaching value. This beautifully illustrated and well-organized book should be of particular value to orthopedists, pathologists, and radiologists. The section on the jaw bones should be of special value to dentists. Gout, a condition of tumor-like appearance, has not been included in this edition. Pathologists generally may object to the use of the word "mis-reading" on pages 90 and 388 to mean false interpretation of the pathological findings on a slide. More and more the word "reading" is coming into use to mean diagnosis of a slide, as if the procedures of preparation of a tissue section culminated with attaching a diagnosis to the coverslip. This is a regrettable oversimplification of the task of a pathologist. Other questionable terms such as "lesional tissue" and "trabeculae" for "trabecula" are unfortunate but not of the same order of seriousness as "mis-reading." These minor defects do not seriously detract from the major contribution which Dr. Jaffe has made in his book. It should find its place as a standard work in its field used alike by orthopedist, pathologist, and dentist.

Lumbar Disc Lesions: Pathogenesis and Treatment of Low Back Pain and Sciatica. By J. R. Armstrong, M.D., M.Ch., F.R.C.S., Orthopaedic Surgeon to Metropolitan Hospital, London. Foreword by H. Osmond-Clarke, C.B.E., F.R.C.S., Orthopaedic Surgeon, London Hospital, London. Second edition. Cloth. $12. Pp. 244, with 81 illustrations. Williams & Wilkins Company, 428 E. Preston St., Baltimore 2; E. & S. Livingstone, Ltd., 16 and 17 Teviot Place, Edinburgh 1, Scotland, 1958.

This monograph is well written and illustrated with line drawings, photographs, and reproductions of roentgenograms. The first two chapters, devoted to the anatomy and the functions of lumbar intervertebral disks, present the best descriptions that have so far been written. Of particular importance, however, are the chapters related to the pathological changes in lumbar disk lesions. The author clearly shows the various stages of degeneration that take place in a disk and particularly the changes that may take place before true herniation occurs. This prepropulsion or preherniation stage could be generally termed the degenerative phase of disk pathology in contrast to the true herniated phase. The next sections, devoted to the clinical findings and the differential diagnosis of lumbar disk lesions, are extremely comprehensive. The latter portion of the book is devoted to treatment: first, the conservative treatment with which there is relatively little disagreement and, second, the operative treatment. There are many illustrations, with beautifully colored drawings, but there are also points of minor controversy, such as areas of lamina to be removed and duration of postoperative bed rest. These minor defects in no way detract from the general excellence of this book. It is definitely recommended for all who are doing disk surgery and is an excellent reference book for those in training.

Neue Ergebnisse der Nervenphysiologie. Sechs Vorträge. Von Alexander v. Muralt, Dr. med. et phil., Professor für Physiologie an der Universität Bern. Mit einem methodischen Anhang. Gemeinsam bearbeitet mit Prof. Dr. med. Silvio Weidmann. Cloth. 49.80 marks. Pp. 269, with 158 illustrations. Springer-Verlag, Reichpietschufer 20, (1) Berlin W. 35 (West-Berlin); Neuenheimer Landstrasse 24, Heidelberg; Göttingen, Germany, 1958.

This book, which is based on lectures given by the author on various occasions in Europe and the Americas, consists essentially of five sections dealing with the chemistry and physics of nervous excitation, the theory of nervous conduction, the role of thiamine in nervous excitation, and the study of degeneration and regeneration in peripheral nerves. These areas of research in which von Muralt and co-workers have participated for several decades are presented clearly, critically, and enthusiastically. The thorough discussion is aided by numerous excellent illustrations and original diagrams. The chapter on regeneration is of particular medical interest since the author developed new experimental methods involving the cornea and iris of the eye. An understanding of the great variety of experimental procedures used in these investigations is aided by the final chapter (with Weidmann) in which numerous techniques are described. Each chapter is provided with a list of references. There is an adequate index. The work is an outstanding contribution to neurophysiological literature. It is valuable as an introduction to one of the most intricate parts of modern physiology and as an up-to-date review of the physiology of the peripheral nerves.

Operative Surgery. Volume 8: Neurosurgery, Eyes, Ear, Nose and Throat. Under general editorship of Charles Rob, M.C., M.Chir., F.R.C.S., Professor of Surgery, St. Mary's Hospital, London, and Rodney Smith, M.S., F.R.C.S., Surgeon, St. George's Hospital, London. Cloth. $19.50. Various pagination, with illustrations. Butterworth & Co., Ltd., 88 Kingsway, London W. C. 2, England; F. A. Davis Company, 1914-16 Cherry St., Philadelphia 3, 1958.

This is the final volume in a series covering all fields of surgery. The illustrations are numerous and give sufficient detail so that they can be followed with ease. Each surgical procedure is presented in a uniform manner consisting of a description of the preoperative management, the operation, and the postoperative care. The bibliography at the end of each chapter is primarily British and is selective. References from the world literature would prove helpful to students, residents, and fellows. The neurosurgical procedures are primarily those emergency measures that are required as preliminary steps to the transfer of patients to a fully equipped neurosurgical center for definitive treatment. The authors are to be commended for this thoughtful exclusion of major neurosurgical operations. The eye, ear, nose, and throat sections include more operative details, even to laryngectomy with block dissection. There seems to be some inconsistency in the minds of the editors when comparing neurosurgery and neck surgery for cancer. This volume is a pleasure to read. Through cautious editing the usual errors of multiple authorship have been avoided. The book is recommended for postgraduate students, residents, and surgeons in nonteaching centers.

A Bibliography of Internal Medicine: Communicable Diseases. By Arthur L. Bloomfield, M.D. Cloth. $10. Pp. 560. University of Chicago Press, 5750 Ellis Ave., Chicago 37; Cambridge University Press, Bentley House, 200 Euston Rd., London, N. W. 1, England; University of Toronto Press, Toronto 5, Canada, 1958.

The title of this unusual book does not indicate its true nature. It is not simply a bibliography; it is an annotated bibliography and also belongs in the category of medical history. Its compiler clearly indicates that it is designed primarily for students and physicians who need this information, which is brought together in a readable fashion. The 30 communicable diseases are covered in 31 sections. The author chose the earliest, or at times the best, articles published on the infectious disease under consideration. There is an author index. Since the bibliography is complete in practically all of the infectious diseases, and since references are made up to and including the time the book was submitted for publication (December, 1957), it is difficult to understand what process of thought led the author to discontinue the bibliography on such an important subject as poliomyelitis. No references on this disease are given beyond the year 1909. It would seem that the medical student and the clinician would be especially interested in the later developments dealing with the methods of isolating and growing the virus and preparing the vaccine for this disease. In general, the book is excellent and should serve a useful purpose, but it is not recommended for the specialist or the scientist.

Coccidioidomycosis. By Marshall J. Fiese, M.D., F.A.C.P., Director of Health Services, Fresno State College, Fresno, Calif. Foreword by Charles E. Smith, M.D., Dean, School of Public Health, University of California, Berkeley. Cloth. $9.50. Pp. 253, with 33 illustrations. Charles C Thomas, Publisher, 301-327 E. Lawrence Ave., Springfield, Ill.; Blackwell Scientific Publications, Ltd., 24-25 Broad St., Oxford, England; Ryerson Press, 299 Queen St., W., Toronto 2B, Canada, 1958.

This monograph covers all phases of its subject. It is everything that a monograph should be. The author has carefully outlined his subject and has adhered to his outline in detail. Chapters 1 and 2 deal with the current importance of coccidioidomycosis and its historical aspects, and an excellent chapter on the mycology of Coccidioides immitis follows. Chapter 4 deals with the geographical distribution of the organism. Chapters 5, 6, and 7 cover the epidemiology, immunology, and variations in susceptibility to coccidioidomycosis. The next chapter is on the pathology of the disease. Chapters 9 through 14 include its clinical aspects and what is known about treatment. In this part of the book the author also discusses the disease in lower animals. The monograph concludes with a comprehensive chronological bibliography of articles on coccidioidomycosis from 1892 through 1957. The illustrations are excellent and the tables are orderly and readable. This book should serve as a model for those who wish to prepare monographs on specific diseases. It is highly recommended for the teacher, student, and laboratory worker, and it should be in the library of every internist who is interested in infectious diseases.

QUESTIONS AND ANSWERS

CATHETERIZATION PRIOR TO CHILDBIRTH

To the Editor:—*Quite a lively controversy has arisen in a hospital concerning catheterization of patients just before delivery. One group claims that routine catheterization accomplishes nothing of value and may lead to infection of the urinary tract; it is felt that women who did not have catheterization just prior to delivery develop fewer cystoceles than those whose bladder was meticulously emptied at that time. The other group feels that a bladder containing any urine at all is much more subject to trauma during birth of the infant and that fewer cystoceles are seen when routine emptying of the bladder is carried out just prior to extraction of the presenting part. Please give the current view on this subject.* *M.D., New York.*

Answer.—This is a controversial subject, because in most instances it is difficult or impossible to prove a definite relationship between catheterization and subsequent disturbances except infection. Surely, it has not been proved that cystocele is due to catheterization or omission of catheterization just before delivery. The problem of bladder infection after catheterization is nearly always due to improper technique and should not be a deciding factor. In all deliveries, as in all surgical operations, conditions should be as aseptic as possible. It is generally agreed by obstetric authorities that the bladder should be emptied by catheter before forceps deliveries, breech extractions, versions and extractions, and any extensive vaginal manipulation, because an empty bladder permits easier delivery and reduces the risk of injury to the bladder. However, in cases of spontaneous delivery this consultant sees no reason for routine catheterization, particularly because an episiotomy is generally performed which takes considerable pressure off the bladder and urethra by the baby's head. Of course, if the bladder is distended with urine at the time the presenting part is to be delivered, catheterization should be carried out just before delivery.

PHILOSOPHY OF ALLERGIC DESENSITIZATION

To the Editor:—*The ordinary general practitioner is bewildered by the mass of contradictory "information" on allergic diseases and treatment. Persons with chronic allergies, such as dermatitis, asthma, or hay fever, who must receive almost continuous exposure to the offending antigen throughout their symptomatic period, go to the allergist for "desensitization." For some reason, the exposures they are getting do not desensitize them. But they get better—with little or no severe reaction in the desensitization process. Can some reasonably concise and intelligible reconciliation of all the contradictions be made? Most physicians do not have the time to take a residency in allergy or to read a 1,000-page textbook and think it all through.*

Alfred B. Mason, M.D., Concord, Calif.

Answer.—This consultant is in complete sympathy with the questioner. The literature on allergic diseases and their treatment is indeed voluminous, and the views expressed by specialists in the field are often contradictory. The confusion created is further compounded by the extravagant claims of some commercial pharmaceutical firms who attempt to persuade the practitioner that their antiallergy medicine is markedly superior to a similar one advertised by a competing manufacturer. The question as stated can be divided into three parts: 1. Why do patients improve after injections of antigens to which they are allergic, when exposure to the identical antigens by inhalation or contact aggravates rather than ameliorates the symptoms? In effect, what is the mechanism of specific allergic desensitization therapy? 2. What is the effect of emotional factors on allergic disease? Are allergy symptoms purely psychosomatic, are the so-called desensitizing symptoms merely placebos, and is improvement attributable to psychological mechanisms? 3. Is there a concise textbook available which reconciles the apparent contradictions and gives a reasonable and intelligible explanation of the problems involved in the management of patients with allergic disease?. 1. Admittedly, the complete answer to the complex problem of which exact immunological mechanisms are involved in the relief of symptoms after injections of antigens during allergy management is not known. The most acceptable and logical explanation at the present time is the theory of the formation of blocking or neutralizing antibodies during the course of the in-

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The answers here published have been prepared by competent authorities. They do not, however, represent the opinions of any medical or other organization unless specifically so stated in the reply. Anonymous communications cannot be answered. Every letter must contain the writer's name and address, but these will be omitted on request.

jections. That is, parenteral injections of specific antigens to which the patient is allergic will provoke the production of blocking or neutralizing antibodies which are different from the naturally occurring allergic antibodies (reagins). When these divergent antibodies join the specific offending antigens, the resulting reaction is harmless as compared to the conventional antigen-antibody reaction which instigates allergy symptoms. Since all or most of the available invading antigen is used up in this harmless reaction, there is little or none available to react with the reagins and, thus, the symptom-producing antigen-antibody reaction is avoided. 2. It is particularly difficult to accept and understand the thesis of the existence of certain emotional constellations for specific allergic diseases as described in great detail in the literature. Not only allergists but psychiatrists as well differ on this point. Neither, however, deny the profound effects of emotional factors on the symptoms of allergic disease. The symptoms of hay fever, asthma, and allergic dermatitis, for example, can be precipitated, aggravated, prolonged, or perpetuated by psychogenic stimuli. However, this occurs in patients who already have allergic disease or the allergic diathesis. That is to say, the ability to produce purely psychogenic allergic disease *de novo* has not been proved. Allergy desensitization injections, when definitely indicated in the properly selected and diagnosed case, cannot be considered placebo therapy, and the relief obtained is definitely not the product of "unconscious motivation." It would be quite difficult to accept the thesis, as several allergists have pointed out, that hundreds of thousands of ragweed-sensitive patients develop a mass emotional disturbance severe enough to produce hay fever symptoms on the 15th of August each year and that a large percentage of these are made symptom free by a series of placebo injections. 3. Several excellent texts on allergy, which are not voluminous and which do not indulge in excess controversy, have been published in the past. One of the most recent which would best fit the requirements of the questioner is that by Harris and Shure, which was reviewed in THE JOURNAL, Jan. 11, 1958, page 198 (Practical Allergy, Philadelphia, F. A. Davis Company, 1957).

BENIGN POLYP OF THE STOMACH

To THE EDITOR:—*A 63-year-old man in excellent health has an asymptomatic benign polyp of the stomach. What course of action should be taken—elective surgery or periodic x-rays—to determine malignant change?*

Harold B. Lehman, M.D., Charlestown, Ind.

ANSWER.—It might be said that one cannot rely totally on an x-ray examination to determine whether a gastric polyp is benign or malignant. Such a polyp associated with achlorhydria would make one more suspicious of a malignant lesion. Certain studies have indicated that a polyp which is 1 in. or more in diameter is prone to be malignant and that about 80% of such polyps which are asymptomatic are benign. If the polyp is less than 1 in. in diameter, there is adequate gastric acid, and the patient is asymptomatic, some clinicians and surgeons may elect to watch the patient and perform frequent examinations. However, if the patient is in good health and one is to be entirely certain as to the nature of the lesion, the best course would seem to be exploration of the polyp.

POSITIONAL VERTIGO

To THE EDITOR:—*A patient has a chronic back problem primarily on the basis of strain. He states that after he puts in his dentures he is troubled with sore throat, excess salivation, and a feeling of fulness in the throat and ears. This is followed by a period of feeling off balance, and sometimes he can partially remedy this by either taking off his glasses or tilting them at unusual angles by use of such things as match sticks and rubber bands. Consultants have not been able to help. From the objective standpoint, he does have definite rhagades despite vitamin therapy. However, there are no related findings in the pharynx or the mouth. While it is true that this may be a psychosomatic disease, could there be some basic etiology?* *Bert P. Austin, M.D., Utica, N. Y.*

ANSWER.—This is such a weird combination of symptoms (and tricks for their relief) that the problem can hardly be other than of [illegible] gin. This becomes even more like[illegible] has been present for a long time or if there has been a welter of symptoms in the past. The sensations described in the area of the throat and ears are not unlike the so-called globus hystericus. The feeling of being off-balance which follows could represent the giddiness that results from overbreathing induced by fear or anxiety or, perhaps, the spread of afferent impulses into certain brain stem areas. The syndrome is likely to be more fearful to the patient by reason of its having baffled so many physicians. It would appear that manipulation of end organs has produced no useful result and that the time has come to consult a psychiatrist who has a grasp on the dynamics of behavior. One cannot doubt that there is "some basic etiology" to this man's problem; etiologies would be more correct. It seems to require a specialized sort of training to elicit etiological factors of this kind, and few besides psychiatrists—and manifestly not all of them—have garnered this training.

ANSWER.—The answer to this question may well be based on more than observed facts. And the basic facts in the case may also have several facets. This man's chronic backache may have overtones in the unpleasant symptoms affecting his ear, nose, and throat. A feeling of fulness in the throat is closely akin to a lump in the throat, which is often purely hysterical. The excess salivation may be an attempt of the body to reject the unpleasantness of artificial dentures. This consultant has had two such patients in the past five years, treated mostly with placebos since all allergy tests, x-rays, and local medication and treatment were of little value. The new plastic type of dentures were changed to the old-fashioned rubber type of compound, with some improvement. There are cases of mild positional vertigo which may be caused or improved by slight changes—often sudden, minute movements of the head. Thus, changing or altering slightly the position of the glasses, by whatever means, may have an effect on this patient's general well-being. In addition, recent work done in New York indicates the possibility of an acid-base change in such persons, which often causes bizarre symptoms in the nose and throat, with an overlay of vertigo. Sodium thiosulfate in a 10% concentration, 20 drops in water given three or four times a day, may be of value in such cases, and, if not, after a week or so one should change this to treatment with normal butyl alcohol, 7.5% in water, 15-20 drops given three or four times a day. Of course, in spite of all this, there may be a mild or severe psychosomatic overlay, in which case a psychiatrist would certainly be of value.

ANNUAL CHEST X-RAYS

To the Editor:—*In a soybean processing and feed manufacturing plant, employees have for the past six years received annual chest x-rays by a mobile unit. Is the annual chest x-ray procedure desirable or necessary on a mass basis? Is there any likelihood of overexposure to x-rays through this type of procedure, especially if carried out annually over a number of years? How often should such routine tuberculosis screening tests be done for this type of employee? The manufacturing processes in this plant are dusty, although ventilation is usually good, and it has been stated that soybean dust is peculiarly nonirritating to lung tissue.*

James M. Burk, M.D., Decatur, Ind.

Answer.—Annual x-ray inspection of the chest is a good procedure, as it may bring to light evidence of disease in the presymptom stage as well as lesions already causing symptoms. Obviously, a lesion must be macroscopic and of sufficient density to obstruct x-rays before it casts a visible shadow on film. Moreover, it must be located in that part of the lung which is not obstructed from view by shadows of other organs, such as the heart and the diaphragm. Lesions which meet these requirements are usually detectable by shadows they cast before significant abnormal physical signs are in evidence or symptoms appear. Although much has been said and written about dangers of radiation through x-ray exposure, there is no well-documented evidence that the annual examination, such as these employees receive, is harmful. It is assumed, of course, that the mobile unit employed in this plant is equipped with the up-to-date protective devices. However, this subject is being carefully studied. In the meantime, it may be well to limit photofluorograms to persons in whom x-ray inspection is especially indicated. If the screening test is done primarily for tuberculosis, the procedure now being recommended and extensively practiced consists of testing all employees regardless of age with tuberculin and making periodic x-ray film inspection of the chest only of the reactors. This probably would eliminate more than 50% of the employees from the annual film inspection. There is less radiation exposure from making regular x-ray films than from photofluorograms. If the employees are in the age period when malignancy is an important consideration, periodic films of the chest are worthwhile even among the nonreactors to tuberculin. However, no evidence is yet available to show that periodic x-ray films of the chest reveal operable malignancies much more frequently than former methods, although they may be discovered earlier in their course of evolution. Inasmuch as soybean dust has been reported as peculiarly nonirritating to lung tissue, there apparently is no significant dust problem to require periodic x-ray film inspection of the chest.

MINIMUM REQUIREMENTS FOR BLOOD TYPING AND MATCHING

To the Editor:—*What are the present minimum requirements for satisfactory blood typing and blood matching for blood transfusions in a small office laboratory? Is a Coombs' test mandatory in each case?*

Samuel Newman, M.D., Danville, Va.

Answer.—The precautions to be taken when selecting a donor for blood transfusion should be adequate to guard against the occurrence of a hemolytic reaction caused by blood group incompatibility, and this applies to small office laboratories as well as large hospital laboratories. Therefore, tests for the A-B-O blood groups and the Rh_0 factor should be carried out on every prospective recipient. The donor or bank blood selected should be of the same A-B-O group as the recipient, and for Rh_0-negative recipients only type rh (triple Rh-negative) blood should be used. In general, an Rh_0-positive recipient may be given blood which is Rh positive or Rh negative, provided the blood bank screens the serum of all Rh-negative donors to be certain that no Rh_0 antibodies are present. To guard against incompatibilities for blood factors other than A, B, and Rh_0, cross matching tests must be done. Such cross matching tests are of greatest importance in individuals who have had previous pregnancies, blood transfusions, or blood injections of any kind which might have sensitized them to blood factors lacking from their own cells. A number of different methods of carrying out cross matching tests are in use. Antibodies of any given specificity may occur in more than one molecular form, of which the two most important are saline agglutinating (or complete) antibodies and conglutinating (blocking or incomplete) antibodies. No single test will detect both these varieties of antibodies. Therefore, at least one cross matching test should be done to detect the saline agglutinating antibody and at least one to detect the conglutinating or blocking antibody. This entails cross matching tests in a plasma or albumin medium as well as in a saline solution medium. Cross matching tests by the antiglobulin technique should also be carried out where time permits, especially for recipients who may have been sensitized by pregnancy or transfusion, and such tests are indispensable for patients who have a history of previous transfusion reactions. For fuller details concerning the technique of these tests these references may be consulted: Gradwohl, "Clinical Laboratory Methods and Diagnosis" (ed. 5, St. Louis, C. V. Mosby Co., 1956, chap. 5, pp. 994-1189), and "Technical Methods and Procedures" of the American Association of Blood Banks (Minneapolis, Burgess Publishing Co., 1956).

SCLEROSING INJECTIONS FOR WEAK ABDOMINAL WALL

To the Editor:—*A 63-year-old man was operated on for inguinal hernia two years ago. At present, he feels fairly comfortable except that he notices a bulging in the region of the lower part of the scar. The surgeon who performed the operation believes this is due to a weakness of the abdominal wall in that region and not to any leak. The protrusion is visible only when the patient is standing and consists of a flat elevation about 1 cm. high and between 1 and 1½ in. in diameter in the lower half of the scar just above the ligamentum inguinale (pouparti). The situation is well under control with an ordinary abdominal support. Would sclerosing injections in such a case help to strengthen the abdominal wall? If so, is there any danger of the ductus deferens being affected? What else could be done?*

M.D., New York.

Answer.—The description suggests that this patient has a direct inguinal hernia, either a recurrence after repair of a direct hernia or coincidental direct hernia in a patient operated on for oblique hernia. Sclerosing injections have no appreciable value in "weakness of the abdominal wall" and are not recommended. If such injections were made in the vicinity of the spermatic cord, injury to the cord structures might well occur. This would more likely be in the form of occlusion of the blood vessels with resultant swelling and possible subsequent atrophy of the testis rather than injury to the vas deferens itself. The treatment of choice is surgical repair with adequate plastic reinforcement of the posterior wall of the inguinal canal. The only other alternative is the continued use of the abdominal support.

CARBON MONOXIDE AND NERVE DEAFNESS

To the Editor:—*Under what conditions does carbon monoxide poisoning result in nerve deafness?*

M.D., Ohio.

Answer.—Practically all toxicologists believe there is no such condition as the expression "chronic carbon monoxide poisoning" would imply. Carbon monoxide does not accumulate in the body progressively over a long period of time as does, for instance, lead or methyl bromide or silica dust. This fact reduces the question to a consideration of acute carbon monoxide intoxication. This consultant is unable to find, in the American literature, any evidence that carbon monoxide poisoning has produced nerve deafness. Shillito and co-workers (*J. A. M. A.* 106:669-674 [Feb. 29] 1936) examined the records on a large series of cases in the New York City area. The incidence of sequelae was minimal and primarily consisted of psychoses. Henderson and Haggard (Noxious Gases and the Principles of Respiration Influencing Their Action, ed. 2, New York, Reinhold Publishing Corporation, 1943, p. 172) state that most claims of impaired health after exposure to carbon monoxide are unjustified. "They should not be accepted as valid unless all of these conditions can be established: (1) at least a 50% saturation of the blood or a concentration in the air sufficient to induce at least 50% saturation; (2) an exposure of at least three hours; and (3) continuous complete unconsciousness lasting for at least six hours after return to fresh air. Short of conditions of such severity, recovery is practically always complete." In view of these and other observations, it is logical to assume that there exists no relationship between nerve deafness and carbon monoxide exposure.

PROTHROMBIN TIME ESTIMATION

To the Editor:—*Please give an outline for prothrombin time estimation.* *M.D., Missouri.*

Answer.—The method employed successfully in the laboratory of this consultant is that of Quick (*J. A. M. A.* 110:1658-1662 [May 14] 1938) with minor modifications. Blood is obtained by venipuncture and immediately mixed with 0.1 M sodium oxalate in a 9:1 ratio. For the control of anticoagulant therapy, 1.8 ml. of blood mixed with 0.2 ml. of 0.1 M sodium oxalate is ample. The blood is centrifuged to separate the plasma. The determination is carried out as follows: 0.1 ml. of plasma is mixed with 0.1 ml. of thromboplastin suspension and 0.1 ml. of 0.01 M calcium chloride quickly blown into the mixture. The time required from the addition of the calcium chloride to the formation of a clot is measured with a stop watch. With thromboplastin prepared from rabbit brain, a prothrombin time of 12 seconds should be obtained on normal human plasma. A similar value is obtained with use of human brain as the source of thromboplastin. Commercial preparations not made from rabbit brain vary in potency and usually give a prothrombin time longer than 12 seconds. The determination should be carried out in a water bath kept at 37 C. The blood or plasma is kept in an ice bath while the thromboplastin and calcium chloride are placed in the water bath. The results may be recorded in seconds or in percentage of normal. For the latter result, the curve obtained by plotting prothrombin time against prothrombin activity is employed.

NONSUPPURATIVE SCLEROTIC OSTEITIS

To the Editor:—*Please discuss the etiology of osteitis condensans ilii. It has been difficult to locate information regarding this interesting condition. What is found when the involved bone is sectioned?*

Richard L. Siggers, M.D., Eureka, Calif.

Answer.—According to Standard Nomenclature of Diseases and Operations, osteitis condensans ilii is considered as a nonsuppurative sclerotic osteitis. It is coded by completion of the master code 2..-1x6. The condition is marked by an area of dense sclerosis on the iliac side of the sacroiliac joint; the complete code is 2468-1x6.

TESTOSTERONE AND SERUM CHOLESTEROL

To the Editor:—*What is the effect of testosterone regarding atherogenesis?*

Robert A. Heebner, M.D., Compton, Calif.

Answer.—Testosterone, in the recommended dosages, can be used when indicated without deleterious effects in the majority of patients. When used therapeutically, its effect on serum cholesterol is, for practical purposes, negligible.

TREATMENT OF POISONOUS SNAKE BITES

To the Editor:—*Two questions on the treatment of poisonous snake bites, which appeared in* The Journal, *Aug. 30, 1958, pages 2256-2257, warrant further comment. The direction circular heretofore supplied with each package of antivenin (Crotalidae) polyvalent recommended the method that had for many years been approved for management of snake envenomation. In fact, use of mechanical measures—constriction of the envenomated limb with a tourniquet, incisions at the site of the fang punctures and areas of swelling, and application of suction—was for centuries the only method available. Such treatment was based on the theory that venom was disseminated in the body of the victim principally by gradual absorption through the lymphatics. It was contended that much of the venom was probably retained for several hours in the edematous area surrounding the bite; therefore, it was theorized, a considerable amount could be removed by suction applied to incisions of the envenomated tissue. In 1936, Duran-Reynals first demonstrated the spreading of rattlesnake and cobra venoms in the bodies of experimental animals by chemical action; he showed, in 1939, that snake venoms are rich sources of hyaluronidase. Since then, it has come to be realized that permeation of the body of the victim by animal poisons takes place largely by enzymatic activity. Little information is available as yet on the ability of snake venom hyaluronidases to break down mucopolysaccharides other than hyaluronic acid. A number of investigators have studied, and reviewed the literature on, the spreading factors and other enzymes in poisons of animal origin (Venoms, publication 44, Washington, D. C., American Association for the Advancement of Science, 1956). The animal experiments of Leopold and associates* (Mil. Med. 120:*414, 1957) in the research laboratories of the U. S. Marine Corps, at Camp Lejeune, N. C., furnished some interesting information on the inefficiency of mechanical measures for treatment of snake envenomation. Immobilization appeared to retard spread of venom in the tissues of the subject. Use of tourniquets did not increase survival of the immobilized envenomated animals. More local damage developed in the envenomated limbs to which tourniquets were applied than occurred in envenomated limbs of the merely immobilized controls. (Allen [*South. M. J. 31:*1248, 1938;* Am. J. Trop. Med. 19:*393, 1939] had made the same observations 20 years earlier and abandoned clinical use of the occlusive tourniquet.) The U. S. Marine Corps researchers also found that incision and suction not only failed to aid but actually decreased the survival period. They stated, "The pumping and manipulation apparently produced faster venom spread and the animals died more rapidly." Some of the clinical arguments against use of mechanical measures for treatment of snake envenomation have been reviewed by Keegan (406th Medical General Laboratory Manual, June 1, 1958).*

The producers of antivenin (Crotalidae) polyvalent (North and South American antisnakebite serum) have been aware for some time of the experience and opinions of numerous clinical authorities in snake-infested areas. These observ-

ers have expressed the belief that incision and suction have no real therapeutic value for snake envenomation. Use of mechanical measures is merely a survival from an earlier period when there was no other treatment to resort to. D. G. Miller Jr., of Morgantown, Ky., who teaches in two southern medical colleges, practices in a southern rural community, and has had considerable experience in treating snakebitten patients, has stated in a personal communication: "I have long taught that there is no value in incision and suction and that if any significant amount of venom is to be removed locally, early, rather wide excision is required. This would be impossible on foot, ankle, anterior surface of the lower leg, and on the hands and forearms." (These are the most frequent sites of snake bites!) "Wide excision of any suitable body area would, of course, entail subsequent plastic surgery." Others concur with this opinion. The instructions for treatment of snake envenomation included in the antivenin package as now supplied have been revised to conform to present clinical thinking and have been officially approved. Neutralization of the venom with antivenin in adequate dosage is the only measure recommended. The direction circular contains a condensed account of the evidence on the basis of which chilling, by chemical or other means, is officially interdicted as a form of treatment. Cold merely serves to arrest conduction in the sensory nerves; it does not alter the toxicity of the venom.

The source of the toxicity of venom is not definitely known, nor has the mechanism by which any venom produces its toxic and lethal effects been fully determined. Since the work of Slotta and Fraenkel-Conrat in 1938, which suggested that the toxicity of crotoxin, a crystalline protein obtained from the venom of Crotalus terrificus terrificus (tropical rattler), could be the consequence of its enzymic activity, numerous authors have assumed that the action of one enzyme or interaction of several could explain the toxic effects of venoms. However, more recent experimental evidence, as recorded in the book "Venoms," cited above, suggests a different concept: certain snake venoms contain, besides the relatively nontoxic enzymes, protein molecules possessing specific toxic action. Although certain enzymes present in venom damage the victim, they are not, in Slotta's opinion, the real toxins. Goncalves states that it is difficult to answer the question as to whether the diversified symptoms of snake envenomation may be ascribed to one toxin, which may exert various pharmacodynamic actions, or to other molecules; all may be involved. He has described another toxic protein, crotamine, which appears to occur in the venom of C. t. terrificus from southern Brazil only. Slotta contends that crotoxin, a highly complex substance probably composed of several subunits, possesses, in addition to certain enzyme components, one or more separate toxic principles. The Indian workers have isolated from the venom of Naja tripudians (cobra) at least two neurotoxins that show little or no hemolytic activity and several enzymes of which one is strongly hemolytic but practically nontoxic. There is no evidence that clinical use of chilling, although it may somewhat retard certain enzymic functions, will significantly interfere with tissue destruction or reduce the activity of other toxic principles present. Therefore, chilling may be permitted temporarily in an effort to alleviate pain until serum can be administered, but after injection of antivenin application of cold is unwarranted and should be discontinued.

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(Polyvalent antivenin packaged prior to the present time may contain the older instructions. Information regarding the use of antivenin in both sets of instructions remains essentially the same, but all reference to the use of incision and suction has been deleted from the new instructions.—Ed.)

SAFE PARTICIPATION IN SPORTS

To the Editor:—*Under the heading "Safe Participation in Sports," in the Questions and Answers section of* The Journal, *May 10, 1958, page 272, a question pertains to "the incidence of cerebrovascular accidents and other pathological conditions caused by atherosclerosis," with increased occurrence related to aging and "excessive physical or nervous tension." It is asked, "At about what age must physical overactivity, especially certain sports such as gymnastics, be considered as potentially dangerous and therefore restricted?" The consultant replies that no categorical answer can be given.*

The issue can be dealt with much more specifically. Evidence is available to the effect that age per se is virtually without relevance for the clinical evaluation of the effects of physical exercise, including "certain sports such as gymnastics." The justification for this statement is provided in several recent studies, among them the age analysis of participants at the 1952 Olympic games (Jokl and others, Sports in the Cultural Pattern of the World, Helsinki, Finland, 1956). This study showed that median ages for participants in the various competitions ranged from 21 (400-meter free-style swimming) to 42 (dressage). The total age range was 13 (400-meter and 1,500-meter free-style swimming) to 66 (clay pigeons). Ages of first, second, and third place winners ranged from 17 (clay pigeons; silhouette, 60 shots; 62-kg. free-style wrestling; and 1,500-meter free-

style swimming) to 58 (dressage). Significant data were also obtained during the 1953 Annual National Gymnastic Festival at Marburg, Germany. Men aged 40-84 and women aged 32-55 performed prescribed exercises on the parallel bars and the horizontal bar, respectively, of a standard of severity far above that of which untrained university students aged 18-22 were found capable in a control investigation (Jokl, Alter und Leistung, Berlin, Springer-Verlag, 1954).

Evidence has also shown that the regression of physical efficiency levels of untrained subjects, as is found with advancing age in respect to athletic performance, can be readily nullified by systematic training. Thus, champion gymnastic, tennis, mountaineering, equestrian, and long-distance running feats have been performed by persons in their 50's and 60's. Conversely, a critical decline of physical efficiency, due to lack of training, was reported by Col. L. G. Rowntree, Chief of the U. S. Selective Service System during World War II, for the majority of inductees under 30 years of age.

The question of the impact on pathological states of the physiological adaptations which take place in response to exercise and training is of axiomatic significance and therefore does not apply specifically to the older age groups. That the incidence of atherosclerosis is higher in old than in young people is, of course, true, but the issue as such is the same as that concerning young people with atherosclerotic disease who subject themselves to exercise and training. In both, exercise and training can bring about compensation or can even reverse the functional sequelae of the illness if it is so treated early, as recent studies from my laboratory have demonstrated (Am. Heart J. 54:556, 1957). *Fatal collapse associated with physical exertion has been observed in children, as is illustrated in the case of a 10-year-old boy who died after exercising* (Lancet 2:659, *1944). Photomicrographs from the coronary artery showed an occluded left descending branch with an organized thrombus containing small vessels, indicating long-term adaptation, and, in a different portion of the thrombus, extravasated erythrocytes, calcium deposit, and thickened media. However, "excessive physical or nervous tension" due to "physical overactivity," to which the inquirer refers, never plays a primary role in such dramatic occurrences. The exercise situation, as such, cannot be considered the cause of death in these cases, just as the bed does not exert a specifically deleterious influence on patients who die from cardiovascular causes during sleep.*

Data are also available to show that regular exercise has a distinctly favorable prophylactic effect on the degenerative diseases of the heart and arteries and, in time to come, that it will also play an increasingly important role in therapy. However, two facts have to be realized in this connection: 1. In the United States very few middle-aged and elderly persons keep themselves fit. 2. Although it is possible in many cases of the kind under review to reestablish a higher level of fitness, even after prolonged periods of inactivity, such an effort presupposes medical supervision on the basis of special knowledge of clinical medicine, as well as of physical education such as very few physicians currently possess. Of course, many say and write that they do.

In conclusion, I must concur with the consultant in adopting a conservative attitude—not necessarily because of inherent desiderata arising out of the situation but mainly because the medical profession has not yet received, through medical schools and research institutions, the required information and indoctrination.

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PROPHYLAXIS FOR POISON IVY

To THE EDITOR:—*In the Questions and Answers section of* THE JOURNAL, *Oct. 18, 1958, page 979, the consultant mentions the use of poison ivy leaves in prophylaxis. Many patients have chewed these leaves and have had no ill effects. But one, when seen a few hours later, was almost choking to death and required several days for recovery. Her mouth, pharynx, and epiglottis were so swollen and edematous that for a while it was thought that a tracheotomy would be necessary. Such a measure is to be noted and advised only under the most careful circumstances. Some persons might consider a brief mention of it by the consultant (who obviously had not tried it himself) to be a recommendation. I consider such recommendation to be dangerous, and I write this to let other doctors know that such is the case.*

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The above comment was referred to the consultant who answered the original question, and his reply follows.—ED.

To THE EDITOR:—*There was no intention on the part of this consultant to recommend chewing poison ivy leaves as a means of producing prophylaxis in poison ivy dermatitis; it was meant merely to indicate, as a matter of history, that this procedure "was reported among the American Indians more than 150 years ago." Although even today farmers are said to chew a leaf occasionally as a prophylactic desensitization measure, it certainly is hazardous, as indicated in the comment, and not to be recommended.*

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STUDY OF STAPHYLOCOCCIC INFECTIONS OCCURRING ON A SURGICAL SERVICE

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Two 60-bed general surgery wards were compared as to the incidence of staphylococcic infections. In one ward, only routine precautions were taken against the spread of infections. The other ward was treated as nearly as possible like an isolation unit, with special bedding, dressing carts, and other facilities. Of 74 patients who acquired staphylococcic hospital infections during the one-year period, 41 were in the latter ward, and the semi-isolation techniques that had been used were found completely inadequate for the control of staphylococcic infections on surgical wards. Valuable data were obtained by culturing the organisms and classifying them according to coagulase reaction, antibiotic resistance, and bacteriophage type. The withdrawal of a given antibiotic for eight months was not sufficient to affect the antibiotic-resistance of prevailing strains, probably because the drugs used in any given hospital were but a fraction of those used in the community from which the patients came.

IN RECENT years increasing numbers of reports have appeared in the literature in regard to the seriousness of hospital acquired staphylococcic infections, the resistance of these organisms to the antibiotic drugs in common use, and the application of the bacteriophage-typing technique for determining the relationship of cultures from different sources.[1]

Our attention was first called to this problem while we were attempting to evaluate the cause of ever increasing numbers of cases of staphylococcic enteritis occurring on surgical wards.[1a] Although we had not experienced an actual outbreak of surgical staphylococcic infections, we were aware of the presence of sporadic cases. On this basis we decided to investigate the source of these infections, focusing our attention on the staff and personnel carrier as a potential source of cross infection, and to determine, if possible, ways and means of preventing the dissemination of Staphylococcus pyogenes var. aureus on the surgical wards.

Methods and Materials

In order to evaluate the possible benefits of simple semi-isolation techniques as a means of controlling spread of cross infection, two general surgery wards of 60 beds each, nearly identical in

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physical structure and situated one above the other, were selected for study. One was established as a study ward, the other as a control ward. In the former, private and semiprivate rooms at one end were divided from the ward proper by double doors. This area was equipped with special bedding, dressing cart, utensils, and hand washing facilities and was as far as possible established as an isolation unit.

All patients who were admitted with infections and those who developed infections during hospitalization on the study ward were placed in this area. Personnel caring for these patients wore caps, gowns, masks, and gloves, and strict aseptic technique was used when dressings were being changed. However, the same personnel were responsible for the care of patients on the remainder of the ward, which included seven-bed rooms divided into admission and postoperative rooms. On the control ward, precautions other than those routinely used were not employed. A continuous record of each patient, in relation to time, place, contact with other patients, and personnel caring for him, was kept throughout the study period.

TABLE 1.—*Phages of Four Groups of Staphylococci and Miscellaneous Groups (Blair) and Phage Patterns Most Commonly Occurring in Our Study*

Group	Characteristic Phages	Common Phage Patterns
I	29, 52, 52A, 79	52
II	3A, 3B, 3C, 55, (39), (523)	3C
III	6, 7, 42E, 47, 53, 54, 70, 73, 75, 77, (42B), (VA4)	53/VA4, 44A, 7, 47/53/54/77/VA4, 77
IV	42D	
Miscellaneous .	44A, 81	44A
Unclassified ..		80/81, 47/42D*

* Formerly reported as 52/42B/81.

Since it has been well established that a great number of staphylococci, indigenous to our hospital, are resistant to the antibiotic drugs in common use, we decided to test the efficacy of the use of "rotational" therapy as a means of delaying or preventing the emergence of drug-resistant strains. As it has been our experience that essentially complete cross resistance occurs between the tetracycline drugs (chlortetracycline, oxytetracycline, and tetracycline) in vitro, we decided to withdraw the use of these drugs for a period of eight months and restrict their use to special requests only. Due to complete cross resistance between these drugs in vitro, they will be referred to as "the tetracyclines" and results reported accordingly.

Bacteriological Procedures.—Nasopharyngeal and rectal cultures were made on a monthly basis of members of the personnel and staff of the two surgical wards under study and the operating suite, and whenever possible on patients on admission, prior to surgery, and on the fourth postoperative day. Stomach and intestinal lumina were cultured at the time of surgery and, in cases of infection, cultures were obtained until the infection had subsided.

All staphylococci isolated were tested for their ability to produce coagulase, either by the use of the biochemical method, with use of Bacto-Mannitol salt agar and/or by their ability to clot citrated human plasma.

Drug susceptibility of pure cultures was determined by the disk-plate method, with use of Sensi-Discs exclusively. The concentrations used were as follows: penicillin and bacitracin, 2 units per milliliter respectively; dihydrostreptomycin, 10 mcg. per milliliter; novobiocin, 30 mcg. per milliliter; and neomycin, chlortetracycline, oxytetracycline, tetracycline, and chloramphenicol, 5 mcg. per milliliter respectively. Strains inhibited by these respective concentrations were classified as "sensitive"; those showing a zone of inhibition of growth of 2 mm. or less were classified as "resistant."

The technique of bacteriophage typing was used to determine the relationship of cultures from different sources. Twenty-five staphylococcic phages were obtained through the courtesy of Dr. John E. Blair and stock cultures and phages were accomplished by the method of Blair and Carr[2] and Blair.[3] Only strong lytic reactions (50 plaques or more) were taken into consideration in reporting of results. Table 1 illustrates the phages of the four broad groups of staphylococci and the miscellaneous groups and the phage patterns most commonly occurring in our study.

Results

During the one-year study period, 74 patients acquired hospital infections caused by coagulase-positive, phage typable staphylococci; contacts were established in 42 of these cases. Forty-one of the patients were located on the study ward and 33 on the control ward. Of cases of cross infection, 24 were located on the study ward and 18 on the control ward. Eleven patients acquired a carrier state at one time or another during their hospitalization.

Included in the hospital acquired infections were 9 preoperative infections (as determined by cultures taken either prior to or at the time of surgery); 44 postoperative wound infections; 7 postoperative complications of other types; and 14 nonsurgical cutaneous infections. Fifty-one patients acquiring infections during their postoperative period indicate an infection rate of 4% (1,350 operations).

Twenty-four patients had infections at time of admission to the wards and 28 patients were nasopharyngeal and/or fecal carriers on admission.

In regard to the staff and personnel of the three study units, carrier rates were as follows: study ward, 34%; control ward, 38%; and operating suite, 40%. Of a total of 114 individual carriers, 49 were nasopharyngeal, 36 were fecal, and 29 were simultaneous nasopharyngeal and fecal carriers. Based on the results of phage typing, 11 of these individuals were "persistent" carriers; that is, they harbored staphylococci of the same phage pattern for a minimum of five consecutive months. Their distribution was as follows: study ward, three; control ward, four; and operating suite, four.

We were unable to demonstrate any significant change in rate of incidence of staphylococci resistant to the three tetracycline drugs, due to a withdrawal of their use for a period of eight months. This phase of our investigation will be reported in detail in a subsequent paper.

One thousand five hundred forty-seven strains of Staph. pyogenes var. aureus were isolated from a variety of 3,632 clinical specimens cultured for this organism. Of these, 56% were coagulase-negative, of which 36% were resistant to penicillin, 19% to erythromycin, 38% to dihydrostreptomycin, 38% to the tetracyclines, and 18% to chloramphenicol. Forty-four per cent of the strains were coagulase-positive, with incidence of drug resistance as follows: 42% to penicillin, 16% to erythromycin, 36% to dihydrostreptomycin, 30% to the tetracyclines, and 17% to chloramphenicol. Strains resistant to bacitracin (12%), neomycin (20%), and novobiocin (17%) were infrequently encountered and therefore will not be further mentioned.

Of 515 strains subjected to phage typing with the 25 phages used, 27% were untypable and 82% were typable with one or more of the phages used. Of the latter, 56% were typable with phages used at the routine test dilution and 15% with phages used at a 1:10 dilution.

Incidence of drug resistance among the untypable strains was 63%, with 26% resistant to penicillin, 21% to erythromycin, 38% to dihydrostreptomycin, 33% to the tetracyclines, and 35% to chloramphenicol. Incidence of drug resistance among the typable strains was 59% with individual drug resistance as follows: 43% to penicillin, 15% to erythromycin, 35% to dihydrostreptomycin, 32% to the tetracyclines, and 15% to chloramphenicol. Of the resistant typable strains, 30% were resistant to a single drug and 65% were multiple resistant.

Table 2 illustrates the incidence of phage patterns in relation to antibiotic susceptibility (372 strains; 33 patterns). Our most commonly occurring patterns were 53/VA4, 44A, 7, 47/42D, 47/53/54/77/VA4, 77, 80/81, 52 and 3C, and these staphylococci accounted for 86% of the total number of strains.

Incidence of drug resistance in the above patterns was 63% with drug resistance as follows: 46% to penicillin, 16% to erythromycin, 37% to dihydrostreptomycin, 35% to the tetracyclines, and 16% to chloramphenicol. Thirty-three per cent of the remaining staphylococci (falling into 24 patterns) were drug resistant.

Table 3 illustrates the relationship of patients with hospital acquired infections and those having infections on admission to the distribution of phage patterns.

Hospital Acquired Infections.—Of 74 patients having hospital acquired infections, 83% were caused by staphylococci of eight of our commonly occurring patterns (53/VA4, 44A, 7, 47/53/54/77/VA4, 77, 47/42D, 80/81, and 3C). However, 39 of the 42 cases of cross infection were caused by staphylococci of the first five patterns. Therefore, our predominant or major hospital patterns were 53/VA4, 44A, 7, 47/53/54/77/VA4, and 77.

TABLE 2.—*Relation of Incidence of Phage Patterns to Antibiotic Susceptibility (372 Strains)*

Phage Pattern	Total No. of Strains	Total No. Resistant	No. Resistant to*				
			P	E	DS	T	Ch
53/VA4†	105	93	76	32	73	54	31
44A	48	27	16	6	15	14	4
7‡	44	20	8	4	4	2	12
47/42D§	37	14	11	0	3	7	1
47/53/54/77/VA4‖	30	16	15	6	11	7	3
80/81	16	14	10	2	4	14	1
77	12	7	3	3	4	6	3
52¶	12	6	6	1	3	4	0
3C#	11	4	2	0	2	2	1
47/81	4	2	1	0	1	0	0
52A/81	3	3	3	0	2	2	1
7/47/53/54/75	3	2	1	1	2	1	1
47/53/54/77/VA4/81	2	2	0	0	2	2	0
81	2	2	2	0	1	0	0
77/44A	2	2	2	0	1	1	0
47/53/77/VA4/44A	2	2	2	0	1	1	0
52/79/44A	2	1	1	1	1	1	0
79	1	1	1	0	1	0	0
523	1	1	1	0	0	0	0
7/VA4/44A	1	1	1	0	1	1	0
52A	6	0	0	0	0	0	0
29/44A	5	0	0	0	0	0	0
47	4	0	0	0	0	0	0
42D	4	0	0	0	0	0	0
70	4	0	0	0	0	0	0
3A/44A	3	0	0	0	0	0	0
42D/44A	2	0	0	0	0	0	0
3A/3B/3C/55	1	0	0	0	0	0	0
7/47/53/73	1	0	0	0	0	0	0
6/73	1	0	0	0	0	0	0
55	1	0	0	0	0	0	0
42B	1	0	0	0	0	0	0
29/47	1	0	0	0	0	0	0
Grand totals	372	220	162	56	132	119	58
% resistant		59	43	15	35	32	15

* P = penicillin; E = erythromycin; DS = dihydrostreptomycin; T = tetracyclines; and Ch = chloramphenicol.

† May be joined by 77 or 47.

‡ May be joined by 77.

§ May be joined by 53, VA4, or 53/VA4.

‖ May be joined by 6.

¶ May be joined by 52A.

May be joined by 3A, 3B, or 55.

In regard to the 28 cases of cross infection of postoperative wounds, of the five predominant patterns, 53/VA4 staphylococci were responsible for 13; 44A for 6; pattern 7 for 3; 47/53/54/77/VA4 for 2; and pattern 77 for 2.

Admission Infections.—Of 24 patients having infections on admission, 17 were caused by staphylococci of six of our commonly occurring patterns (53/VA4, 44A, 47/53/54/77/VA4, 77, 80/81, and 3C). However, 10 of these cases were caused by staphylococci included in four of our predominant patterns. Table 4 illustrates incidence of phage patterns and their antibiotic susceptibilities in relation to the three groups of persons studied.

Table 3.—*Incidence of Patients with Hospital Acquired Infections and Patients with Infections at Time of Admission in Relation to Distribution of Phage Pattern*

Phage Pattern	Pre-operative Infections	Post-operative Infected Wounds	Other Post-operative Infections	Non-operative Cutaneous Infections
Number of Cases of Hospital Acquired Cross Infections (42)				
53/VA4	1	13	2	1
44A	2	6	1	1
7	1	3	1	0
47/53/54/77/VA4	0	2	0	1
77	1	2	0	1
47/42D	0	1	0	0
80/81	0	0	0	1
52A/81	0	1	0	0
Totals	5	28	4	5
Hospital Acquired Infections Lacking Demonstrable Contacts (32)				
53/VA4	0	3	1	2
7	1	1	1	0
77	0	1	0	0
47/42D	0	2	1	3
80/81	0	1	1	1
3C	0	2	0	0
10 less common patterns*	0	5	0	6
Totals	1	15	4	12
Number of Cases of Admission Infections (24)				
53/VA4	1	0	1	1
44A	0	0	0	2
47/53/54/77/VA4	0	0	0	4
77	0	0	0	1
80/81	0	0	0	4
3C	0	0	0	3
5 less common patterns†	1	2	0	4
Totals	2	2	1	19

* Patterns responsible for five postoperative wound infections: 47, 6/73, 42B, 523, and 3A/44A.

† Patterns responsible for two postoperative wound infections: 52/79/44A and 47/81.

Group A represents 122 strains (24 patterns) isolated from cultures from a wide variety of clinical sources from 102 inpatients. Included in this group are 42 patients with hospital acquired cross infections, 32 patients with hospital acquired infections but lacking demonstrable contacts, and 11 patients who acquired a carrier state sometime during their hospitalization. Staphylococci of our five major hospital patterns (53/VA4, 44A, 7, 47/53/54/77/VA4, and 77) accounted for 70% of the total number, and were responsible for 39 of the 42 cases of cross infection.

Incidence of drug resistance in group A was 65%, with 48% of the strains resistant to penicillin, 19% to erythromycin, 45% to dihydrostreptomycin, 44% to the tetracyclines, and 25% to chloramphenicol.

Group B represents 178 strains isolated from nasopharyngeal and/or fecal carriers from the staff and personnel of the study and control wards and from the operating suite. Of these, 152 were nasopharyngeal isolations and 26 were fecal. Staphylococci of our five major hospital patterns accounted for 68% of the total number. Pattern 53/VA4 staphylococci were harbored by 16 carriers, 44A by 12, pattern 7 by 10, 47/53/54/77/VA4 by 7, and pattern 77 by 2. Staphylococci of 53/VA4, 44A, and 7 were harbored by both nasopharyngeal and fecal carriers, whereas those of the remaining patterns were harbored by the former only.

Incidence of drug resistance in group B was 56%, with 38% of the strains resistant to penicillin, 15% to erythromycin, 26% to dihydrostreptomycin, 22% to the tetracyclines, and 10% to chloramphenicol.

Comparison of groups A and B shows that a close correlation exists between phage patterns of staphylococci cultured from patients with hospital acquired cross infections and those exhibited by carriers among the staff and personnel. Although we encountered nine nasopharyngeal carriers among the inpatients, only one played a role in cross infection. Of our predominant patterns, 53/VA4 and 47/53/54/77/VA4 were the only two associated with these patients. Other patient-to-patient contacts, in cross infections, will be discussed later.

Table 4.—*Incidence of Phage Patterns and Their Antibiotic Susceptibilities in Relation to the Three Groups of Persons Studied*

Group	Phage Pattern	Total No. of Strains	Total No. Resistant	No. Resistant to* P	E	DS	T	Ch
A	53/VA4	42	36	31	15	32	25	13
Inpatient strains	44A	16	10	7	3	6	8	3
	7	14	9	1	2	2	2	9
	47/42D	10	4	4	0	3	4	1
	47/53/54/77/VA4	9	3	3	2	2	2	1
	80/81	4	4	4	0	0	4	0
	77	4	2	1	2	2	2	2
	52	1	1	1	0	1	1	0
	3C	2	2	2	0	0	0	0
	Less common patterns	20	9	5	0	7	6	2
Totals		122	80	59	24	55	54	31
% resistant			65	48	19	45	44	25
B	53/VA4	50	45	34	14	29	23	13
Carrier strains	44A	28	13	7	3	7	4	0
(staff and	7	26	9	5	2	1	0	3
personnel)	47/42D	22	10	7	0	0	3	0
	47/53/54/77/VA4	11	8	7	1	5	1	0
	80/81	3	2	0	1	0	2	0
	77	6	4	2	0	2	3	1
	52	11	5	5	1	2	3	0
	3C	2	1	0	0	1	1	1
	Less common patterns	19	1	1	0	0	0	0
Totals		178	98	68	22	47	40	18
% resistant			56	38	15	26	22	10
C	53/VA4	13	12	11	3	12	6	5
Admission strains	44A	4	4	2	0	2	2	1
	7	4	2	2	0	1	0	0
	47/42D	5	0	0	0	0	0	0
	47/53/54/77/VA4	10	5	5	3	4	4	2
	80/81	9	8	6	1	4	8	1
	77	2	1	0	1	0	1	0
	52	0	0	0	0	0	0	0
	3C	7	1	0	0	1	1	1
	Less common patterns	18	8	8	1	4	2	0
Totals		72	41	34	9	28	24	10
% resistant			56	47	12	38	33	13

* P = penicillin; E = erythromycin; DS = dihydrostreptomycin; T = tetracyclines; and Ch = chloramphenicol.

Group C represents 72 strains (21 patterns) isolated from various clinical sources from 24 patients having infections at the time of admission and from 28 nasopharyngeal and/or fecal admission carriers. Forty-five per cent of these staphylococci fell into our five predominant patterns (53/VA4, 44A, 7, 47/53/54/77/VA4, and 77).

Incidence of drug resistance in this group was 56%, with 47% of the strains resistant to penicillin, 12% to erythromycin, 38% to dihydrostreptomycin, 33% to the tetracyclines, and 13% to chloramphenicol.

It is obvious from the foregoing report that our predominating "endemic" pattern was 53/VA4. This pattern included 105 strains, or more than twice as many strains as those occurring in any other single pattern. These staphylococci were responsible for 13 of 28 cases of hospital acquired postoperative cross-wound infections. They comprised 30% of all strains isolated from infected lesions from patients having hospital acquired infections and 30% of all strains harbored by the staff and personnel, including a total of 16 carriers (5 of whom were persistent carriers). In addition they were also harbored by six inpatient and three admission patient carriers. Eighty-seven per cent of the 53/VA4 strains were drug resistant and, of these, 84% were multiple resistant. Furthermore, 46% of all cultures resistant to penicillin and 50% of all cultures resistant to the three tetracycline drugs were of this pattern.

For the purpose of comparison, our second most commonly occurring pattern was 44A, which included 48 strains. These staphylococci were responsible for 6 of the 28 cases of hospital acquired postoperative cross infections of wounds. They comprised 12% of all strains isolated from infected lesions from patients with hospital acquired infections, and 15% of all strains harbored by the staff and personnel, including a total of 11 carriers (2 of whom were persistent carriers). In addition they were harbored by one admission carrier. Fifty-six per cent of the 44A staphylococci were drug resistant and of these, 11% were multiple resistant.

In the 42 cases of hospital acquired cross infections, results indicate that 13 infections had their origin in the operating suite; contacts included two surgeons, five anesthetists, two scrub nurses, and two aides. Twenty-four cases apparently originated from contacts with ward staff and personnel carriers. These included two surgeons (including one listed in the above category), five nurses, and three aides (table 5).

Of 17 cases of cross infection due to 53/VA4 staphylococci, results of phage typing indicate that 2 had their origin in operating suite and 15 in the wards. Of the latter, 10 originated from a single contact of the study ward and 5 from a single contact on the control ward. Both contacts were ward nurses and both were persistent nasopharyngeal carriers and transient fecal carriers of the organism in question.

Five cases of cross infection were traced to patient-to-patient contacts. Four contacts had open cutaneous lesions and one was a nasopharyngeal carrier. Pattern 53/VA4 staphylococci were not concerned in these cases; incriminating patterns were 44A, 47/53/54/77/VA4, 80/81, and 52A/81 (table 5).

Seven cases of auto-infection were included in the group of 32 hospital acquired infections lacking demonstrable contacts. The responsible staphylococci were included in patterns 53/VA4 (2 cases), 3A/44A, 80/81 (2 cases), 52A/81, and 3C.

Comment

Results of this investigation indicate that our infection rate (4%) is lower than that reported by Jeffrey and Sklaroff[1m] in a similar study (9%). Our infection rate seems favorably low, especially when we take into consideration that 38 of our 51 patients with postoperative infections had major surgery, the operations requiring two to five hours. Furthermore, all patients were males and 70% were over 50 years of age. Incidentally, 36 of these patients received antibiotic drugs prophylactically and/or therapeutically. Six patients received drugs on the latter basis, to which their respective strains were resistant in vitro.

TABLE 5.—*Professional Status of Carrier Contacts in Relation to Number of Cases of Cross Infection*

Professional Status of Carrier	No.	Cross Infection Cases, No.
Operating Suite		
Surgeons	2	2
Anesthesiologists	5	7
Scrub nurses	2	2
Aides	2	2
Study ward		
Ward surgeons	1	2
Nurses	3	12
Aides	1	1
Control ward		
Ward surgeons	1	1
Nurses	2	6
Aides	2	2
Patient-to-patient contacts	5	5

Since a greater number of cross infections occurred on the study ward than occurred on the control ward, we conclude that the practice of semi-isolation techniques was completely inadequate for the control of spread of staphylococcic infections on surgical wards.

The results of the use of rotational therapy as a means of delaying or preventing the emergence of drug-resistant staphylococci were equally disappointing. We were unable to demonstrate that the withdrawal of the use of tetracycline drugs, for a period of eight months, in any way influenced the rate of incidence in recovery of resistant strains. This is not too surprising when one considers that the amount of those drugs used in our hospital represents but a small fraction of their use throughout the area from which we draw patients, a premise substantiated by 33% of our admission strains being resistant to the drugs in question.

We were able to establish, by phage typing of cultures, a correlation between phage patterns of staphylococci responsible for hospital cross infections and those exhibited by staff and personnel carriers of both wards and the operating suite. In the past, much attention has been focused on the nasal and nasopharyngeal carrier as the main source of spread of infection in hospital populations.[4] However, little attention has been focused on the fecal carrier. Brodie and his associates [1e] emphasize the importance of the latter among hospitalized patients as an added potential source of infection; the authors call attention to their presence among the surgical staff and personnel. If our search for carriers had been based solely on nasopharyngeal isolations, 31% of our 114 carriers would have been completely overlooked as well as the interesting phenomenon that the nasopharyngeal carrier is frequently a simultaneous fecal carrier.

The problem of control of staff and personnel carriers remains a difficult one. We have no new ideas to offer but reemphasize the need for a diligent search for carriers on the basis of phage typing of cultures. The fact that 65% of our inpatient strains and 55% of our carrier strains were drug resistant suggests that the acquisition of these organisms by the latter group is primarily a matter of their availability within a given area. Consequently, the strict practice of aseptic techniques in the handling and care of patients should result in a lowering of carrier rate, and a subsequent reduction in the number of cross infections due to resistant staphylococci.

Although we did not encounter any cases of bacteremia in our series, four deaths were included in which coexisting staphylococcic infections were considered to be a contributing factor. Our problem concerned sporadic cases rather than an actual outbreak of staphylococcic infections. What then is the effect of such cases occurring on a surgical service? Our experience agrees with that reported by Jeffrey and Sklaroff [1m] that the primary effect is economic, brought about by prolongation of hospital stay. For example, occurrence of cross infections of postoperative wounds in 18 of our patients resulted in a total increase in hospital stay of 432 days beyond the usual time required for hospitalization, or a mean of 24 days per patient. The financial impact of such a situation is apparent.

We found little evidence to support the reasoning that inpatient nasopharyngeal carriers of coagulase-positive staphylococci serve as a potential source of cross infection. On the other hand, patients having open cutaneous lesions present a real hazard as sources of cross infection on surgical wards.

It has been frequently emphasized in the past [1f] that, in any particular hospital, the important staphylococci may belong to only a few phage patterns carried in the anterior nares or nasopharynx of the staff and personnel. Such has been our experience, the important staphylococci in our series belonging to 5 of 33 patterns. Furthermore, staphylococci of each of the five important patterns were also introduced into the wards from outside sources. Our results also indicate that staphylococci of our "predominant" or "endemic" pattern (53/VA4) were endowed with enhanced powers of communicability, infectivity, and resistance to the antibiotic drugs in common use.

The universal observation that the majority of drug-resistant staphylococci belong to broad group 3 correlates with our results. Of 220 drug-resistant strains, 62% belonged to this group. However, drug-resistant staphylococci were also encountered in each of the remaining groups.

Since 1954 the dissemination of 80/81 staphylococci in the United States has been wide and rapid. As a result, these organisms are causing particular concern throughout the country. However, the chief concern has been limited to outbreaks of infections in nurseries and in outbreaks of breast abscesses in nursing mothers. Although staphylococci of this pattern were included in our nine commonly occurring patterns, they were of little or no significance in cross infections (only 1 in 42 cases, and this a nonsurgical cutaneous infection). It is pertinent to mention that the patients from whom these particular staphylococci were recovered were all males, with the majority over 50 years of age. Thus it would seem that these strains have a special predilection for the newborn infant and nursing mothers.

It is regrettable that we were unable to subject all of our cultures of coagulase-positive staphylococci to phage typing. During the first four months of the study period, we were handicapped by lack of adequate technical assistance and subsequently lost a number of stock cultures due to contamination on refrigeration.

Conclusions

The problems of control of staff and personnel as contacts in cross infection and the prevention of emergence of drug-resistant strains have not been solved by the results of our investigation. They remain extremely difficult problems. Certainly they call for strict practice of aseptic techniques and for the conservative and intelligent use of the antibiotic drugs at our disposal.

For a better understanding of the pathology, epidemiology, and chemotherapy of hospital acquired staphylococcic infections occurring on a surgical service, it is necessary to determine the drug susceptibility and phage patterns of each strain cultured from inpatients and admission pa-
and personnel.
tients, as well as from periodic cultures of the staff

West National Avenue at 54th Street (Dr. Smith).

Mrs. Lorraine M. Kastensen and Mr. Abe Resnick gave technical assistance for this study.

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TREATMENT OF HYPERTENSION WITH CHLOROTHIAZIDE

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When chlorothiazide is used, lower and, hence, less toxic dosages of other hypertensive agents become effective in controlling blood pressure. Chlorothiazide does not reduce blood pressure in normotensive subjects, although the drug induces the same increase in salt excretion. Regarding the mechanism of antihypertensive effect of chlorothiazide, it may be tentatively concluded that the blood pressure reduction accompanies the salt loss and probably is a consequence of it. When chlorothiazide is added to the regimen of a patient taking ganglionic blocking agents, the dosage of the latter must be reduced by half. The responsiveness of the patient is so remarkably increased by chlorothiazide that, if full dosage is continued, severe hypotension, including postural collapse, usually will occur. The other so-called toxic reactions to chlorothiazide are only extensions of its fundamental saluretic and kaluretic actions. Hypopotassemia is frequent, and potassium supplements should be used when this develops.

After more than a year of clinical trials, chlorothiazide has become established as a valuable agent for the control of hypertension.[1] It is an especially important drug in general practice, because it can be administered according to straightforward dosage schedules and, in the presence of uncomplicated hypertension, has been relatively free of toxic reactions. Indeed, it has reduced the over-all incidence of toxicity and side-effects of antihypertensive drug therapy. When chlorothiazide is used, lower and, hence, less toxic dosages of other hypertensive agents, such as hydralazine or the ganglion blocking drugs, become effective in controlling blood pressure. The special circumstances under which toxicity can occur will be discussed later.

Mechanism of Effects

Previous reports from this laboratory[2] stressed the importance of salt loss in the mechanism of the antihypertensive effects of the drug. This view has been contested by Wilkins and co-workers.[3] However, further work in this laboratory in the interim has only strengthened the initial observations. These studies may be reviewed briefly here. When chlorothiazide was given to nonedematous, hypertensive

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Read in the Symposium on the Newer Diuretics—Especially Chlorothiazide—Indications and Reported Use before the Section on General Practice at the 107th Annual Meeting of the American Medical Association, San Francisco, June 26, 1958.

patients, a urinary loss of approximately 250 mEq. or roughly 1.5 Gm. of salt occurred primarily in the first 24 to 48 hours after the drug was administered. This depletion seemed to be derived in large measure from the extracellular fluid, since measurements of this space disclosed reductions of 1 to 2 liters. Accompanying the diminution in extracellular fluid space was also a reduction in plasma volume (fig. 1). The reduction in plasma volume had also been observed by Tapia and associates.[4] At the same time that these events occurred, the blood pressure fell. It did not precede the saluresis (urinary loss of salt) or follow days later.

These changes were not peculiar to chlorothiazide. They occurred also with ammonium chloride plus mercurials. It is as if well-compensated individuals are, in effect, slightly edematous. At least there seems to be an easily mobilized pool of extracellular fluid which can be skimmed off by saluretic drugs. Another point that leads one to believe that the antihypertensive effect of such agents is secondary to the salt loss is that if sufficient salt is given (and this may require as much as 25 Gm. per day) the antihypertensive effect of the drug is at least partially overcome.

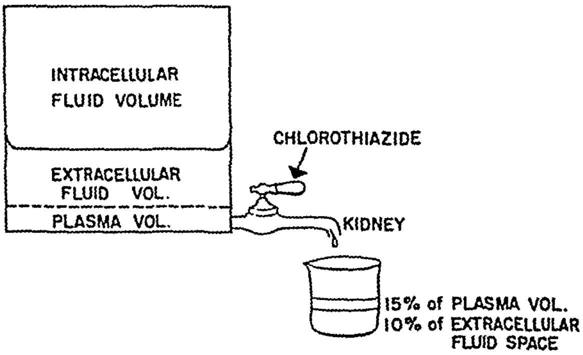

Fig. 1.—Effect of chlorothiazide in nonedematous patients.

Interestingly enough, chlorothiazide does not reduce blood pressure in normotensive subjects, although the drug induces the same increase in salt excretion. However, Dr. A. Wanko, in this laboratory, has shown recently that it changes vascular responsiveness in normal persons even though basal blood pressure is not altered.[5] The pressor response to arterenol is decreased, and the depressor response to ganglionic blocking agents is increased. Most important of all, the vascular responsiveness reverts back to pre-chlorothiazide-therapy levels when the plasma volume is restored with 500 ml. of a 6% solution of dextran.

Dr. I. M. Wilson, also in this laboratory, has carried out repeated determinations of plasma volume and extracellular fluid space in hypertensive patients treated for long periods.[6] She finds that some reduction persists until the drug is withdrawn, after which the volumes rise promptly to pretreatment levels.

At present, therefore, regarding the mechanism of antihypertensive effect of chlorothiazide, it may be tentatively concluded that (1) it has no unique hypotensive properties not shared by other saluretic agents, such as the mercurials; (2) the blood pressure reduction accompanies the salt loss and probably is a consequence of it; (3) the salt loss comes primarily from the extracellular fluid, and the drug produces a sustained reduction of extracellular fluid space and plasma volume; and (4) the reduction of plasma volume and of tissue pressure due to the extracellular fluid loss may play a role in reducing the basal blood pressure of hypertensive but not of normotensive persons and of vascular reactivity in *both*.

Combined Therapy

It is this increased responsiveness to depressor stimuli that makes chlorothiazide an effective agent in the management of hypertensive patients. By itself, it has only a moderate effect on blood pressure in most patients. But when any type of antihypertensive agent is given in conjunction with chlorothiazide, it gains a new depressor effectiveness. This is particularly true in the case of the ganglionic blocking drugs and of hydralazine (Apresoline) hydrochloride. Because dosages need be less, treatment becomes not only more effective but also simpler, since it is no longer necessary to skirt on the edge of toxic dose levels.

In order for maximum benefit to be obtained from chlorothiazide it must be remembered that hypertensive patients differ in their responsiveness to antihypertensive medicaments. For example, in a random group of 100 hypertensive patients, 20 of those with milder degrees may respond satisfactorily to chlorothiazide alone, 20 others to chlorothiazide and Rauwolfia preparations, and 40 to chlorothiazide and hydralazine, while the final 20 may require the ganglionic blocking drugs, at least for a time. Which of these combinations approaches most closely the ideal of general effectiveness, safety, tolerability, and simplicity? Experience here would indicate that in all forms of mild and moderate hypertension which merit any treatment at all the nearest approach to the ideal is represented by chlorothiazide and hydralazine.

The dosage of chlorothiazide in patients with hypertension uncomplicated by cardiac or renal failure can safely be 500 mg. given twice daily on arising and at bedtime. This will be an effective saluretic dosage in practically all patients, and it avoids the needless complications of titration. In this clinic, patients with uncomplicated hypertension have been given this dosage continuously for more than one year without toxic effects. To this is added 25 mg. of hydralazine two or three times daily. If this dosage is insufficient, it is raised to 50 mg. three times daily but not beyond this level, since toxic effects can occur at higher dosages. Unlike some other antihypertensive drugs, this combination does not produce easy fatigue, lethargy, or mental dulling. One avoids the considerable danger of precipitating an emotional depression in intellectual persons who are given Rauwolfia, as well as the inconvenience of dosage juggling so frequently required with the ganglionic blocking drugs. Of course Rauwolfia, the ganglionic blocking agents, or both are added whenever the chlorothiazide-hydralazine regimen is ineffective. Dosage readjustments of the blocking drugs are not as frequently required in patients who are also taking chlorothiazide. In addition, the side-effects of ganglionic blockade are far less, due to the lower dosage requirement.

Toxic Reactions

It is necessary at this point to emphasize that, when chlorothiazide is added to the regimen of a patient taking ganglionic blocking agents, the dosage of the latter must be reduced by half. The responsiveness of the patient is so remarkably increased by chlorothiazide that, if full dosage is continued, severe hypotension, including postural collapse, usually will occur. For the same reason, care must be used in administering chlorothiazide to a patient who has previously undergone sympathectomy. This usually is well tolerated, but if such a patient is elderly or has arteriosclerosis there is the possibility of precipitating a coronary or cerebrovascular occlusion if the hypotensive response is marked.

The example just cited could be called a "toxic effect" of chlorothiazide, since the net result is deleterious to the patient. But in a more real sense it is not a failing of the drug, whose purpose is to lower blood pressure, so much as it is a reflection on physicians who proceed thoughtlessly in a situation where wisdom cautions otherwise. The blame in this case is not with the drug but with the physician's judgment.

Similarly, the other so-called toxic reactions to chlorothiazide hold no surprises but are only extensions of its fundamental saluretic and kaluretic actions (fig. 2). The most common of all the "toxic reactions" is hypopotassemia. In patients with uncomplicated hypertension, reductions of serum potassium levels to 3 mEq. per liter is almost commonplace and, in experience at this laboratory, has not been attended by clinical manifestations of hypokalemia or by any evidences of renal damage. The situation in a cardiac patient, on the other hand, has been quite different. Patients with resistant congestive heart failure appear to be potassium "losers," and the addition of chlorothiazide may tip the scale toward critical depletion. This clinical situation is further embarrassed by the fact that digitalis toxicity develops so readily in the presence of hypopotassemia. The first sign of trouble then may be the arrhythmias of digitalis intoxication.

Various measures may be taken to cope with this toxic development. The dosage of digitalis may be reduced or omitted, chlorothiazide may be given intermittently rather than continuously, or potassium supplements may be administered. I do not share the equanimity of other workers regarding the effectiveness of potassium supplements, since they may provide a false sense of security. Chlorothiazide is quite effective in removing excessive sodium in the diet and may do the same with potassium supplements. How much potassium is enough to raise the blood potassium level, and what happens when the patient forgets to take his supplement? These important questions need to be resolved, and it would seem advisable to supply an ample excess of 75 to 100 mEq. orally per day in all patients who develop hypokalemia. There is some evidence to suggest that the hypokalemia may be due to a secondary stimulation of aldosterone secretion.

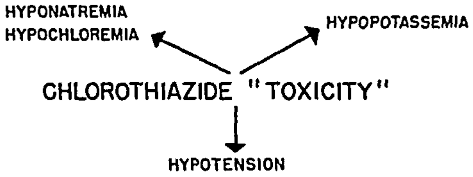

Fig. 2.—Reactions to chlorothiazide as extensions of its fundamental actions.

In the patient who has congestive heart failure secondary to hypertension, it is usually possible to control the failure without digitalis after the blood pressure has been reduced and reaccumulation of edema prevented by chlorothiazide plus other hypotensive agents. There is no need to make a fetish of digitalis if it is harmful in a particular situation. A cautious trial of withdrawal after compensation has been restored will not subject the patient to any significant risk.

In the patient with congestive heart failure due primarily or completely to causes other than hypertension, it is our practice to continue digitalis therapy but to administer chlorothiazide intermittently (usually two days on treatment and two days off), thereby permitting nature to make its own compensations. Unfortunately, in patients with hypertension chlorothiazide must be taken daily, as the blood pressure rises promptly (within 24 to 48 hours) after the drug has been withdrawn.

By the same token, the physician should resist the temptation to give chlorothiazide for correction of hypertension or edema secondary to hyperadrenocorticism, either the naturally occurring varieties or the type induced by steroid treatment. The adrenal cortical hormones conserve sodium and waste potassium. Chlorothiazide increases the excretion of both. In the patient with potassium depletion and hyperadrenocorticism, the additional insult of chlorothiazide may precipitate severe hypokalemia. Similarly, protracted diarrhea, various renal tubular disorders, and ureterosigmoidostomy may in themselves produce potassium depletion and hence make chlorothiazide therapy dangerous. Fortunately, these are situations that rarely arise in the routine management of hypertensive patients.

It is surprising that hyponatremia and hypochloremia do not develop more frequently. There seem to be few authenticated cases, and these conditions have not been observed in this clinic. Once the labile pool of extracellular fluid has been skimmed off, chlorothiazide seems to become relatively ineffective in removing further sodium or chloride. Nevertheless, it would be adding insult to injury to give chlorothiazide in the presence of nephritis with salt loss, or of depletion of body stores of sodium or chloride, as can occur with protracted vomiting or severe diarrhea. On the other hand, last year patients treated with chlorothiazide at this clinic lived through the usual hot Washington summer without any evidences of salt deficiency.

One further word is required on the subject of "toxic reactions" to chlorothiazide. As organic renal damage progresses, the kidney vasculature loses its flexibility in adjusting to a reduced level of blood pressure. When blood pressure falls, glomerular filtration decreases. In the patients with elastic renal blood vessels, adjustments are made quickly so that filtration pressure is restored. But in the rigid vasculature of the patient with far-advanced nephrosclerosis or nephritis, these adjustments are poorly made, with the result that filtration pressure and filtration rate become lower and remain reduced. Such kidneys can ill afford this insult, since they depend on a high urine volume to hold uremia in check. As the filtration rate falls, oliguria develops and nitrogenous products accumulate in the blood.

In the presence of such renal damage and a high level of blood pressure, the physician truly must steer carefully between Scylla and Charybdis. If he aims toward hypotension, he must be aware of the possibility of uremia. But if he withholds therapy, his patient may be drawn further toward malignant hypertension. The only solution then is to proceed cautiously but firmly in the direction of moderating the level of blood pressure, watching scrupulously for oliguria, lightening treatment when this occurs, but pressing forward again watchfully when the danger has passed. Thus, judiciously the physician directs his course altering direction from time to time as prevailing conditions dictate. Few of these patients will be saved even under these circumstances. But the few who are makes the effort worthwhile.

Very often the level of blood urea nitrogen or nonprotein nitrogen will gradually rise. Even in these circumstances, I have persisted for a time, at least, hoping for the occasional instance in which the levels will stabilize and then gradually recede as the patient adjusts to the lower level of blood pressure.

Conclusions

The various complications to chlorothiazide therapy are not common in general practice, but awareness will aid in their prevention. Actually, the good produced by chlorothiazide far outweighs its harm. The discovery of this agent represents a therapeutic advance of considerable significance. The patient with uncomplicated hypertension who does not have congestive heart failure, renal failure, or steroid-induced hypertension has little to fear and much to gain from the use of this drug.

The goal of complete control of elevated blood pressure grows ever nearer. Will this prevent the organic complications that produce morbidity and mortality? I believe it will, but only time and thoughtfully planned studies will provide the final answer.

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CHLOROTHIAZIDE (DIURIL)—A NEW, NONMERCURIAL, ORALLY GIVEN DIURETIC

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and
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The diuretic effects of chlorothiazide were studied in four groups of patients with various degrees of congestive heart failure. All but 2 of the 50 patients were fully digitalized, and all were being kept on diets yielding 1 Gm. of sodium chloride per day. The usual dose for long-term therapy was found to be 250 or 500 mg. given thrice daily by mouth at roughly six-hour intervals for three or four consecutive days a week. Some individualization was necessary. Three case histories illustrate the gratifying results obtained in some patients; a fourth illustrates the fact that patients resistant to mercurial diuretics are generally resistant to chlorothiazide also. Under the conditions of this study, with the use of ammonium chloride and potassium chloride when indicated, no serious electrolyte imbalance occurred, and patients remained free from gastrointestinal and neurological symptoms of toxicity.

Clinical observation concerning a new, nonmercurial, orally given diuretic, designated by the generic name chlorothiazide,[1] constitutes this report. It is designated chemically as 6-chloro-7-sulfamyl-1, 2,4-benzothiadiazine-1,1-dioxide.

It is not primarily a carbonic anhydrase inhibitor [2] but seems to possess the factor of exerting considerable influence on the renal tubular transport of electrolytes, causing a marked decrease in the reabsorption of sodium and chloride and, to a lesser degree, potassium and bicarbonate.[3] The loss of sodium is apparently equal, mol for mol, to that of chloride.[3a] When given in large doses, it is reported [3a] that bicarbonate is lost in "appreciable" amounts, though never to the point of metabolic acidosis as in the case with carbonic anhydrase inhibitors. Smaller but effective diuretic doses produce only relatively minor loss of bicarbonate.

The drug is rapidly and well absorbed when given by the oral route, with onset of action within two hours and a duration of action of somewhat less than 12 hours.[4] The pattern of electrolyte excretion, with marked chloruretic effect and rapid onset, suggested a similarity to mercurial diuretics and, further, that pretreatment with ammonium chloride might enhance its effect and protect the patient from hypochloremic alkalosis.

Methods

Chlorothiazide (Diuril) was employed in several different groups of patients. All were kept on diets with 1 Gm. of sodium chloride, and all but two were fully digitalized. All other diuretic agents were withdrawn except ammonium chloride. There was a total of 50 patients in the study, which covered a period of seven months. All patients were in congestive failure at the time of drug administration. Since the completion of the study, an additional six months of use has occurred, making in all a 13-month period during which the drug has been employed.

Since chlorothiazide was reported[3] to cause a marked chloruresis, several patients were studied by a check of serum electrolyte disturbances. As the study progressed, routine determinations appeared unnecessary, since apparent protection against hypochloremia could be provided simply by ammonium chloride administration. The latter was given in 1-Gm. doses four times daily on three to four consecutive days per week, as with the mercurial diuretics. The substitution of enteric coated potassium chloride for ammonium chloride, 1 Gm. given three times daily for three days, may more completely protect the patients from chloride and potassium loss. The use of ammonium chloride, while it did protect the patient from hypochloremia and alkalosis, did not materially add any diuretic effectiveness and did not appear to enhance the effect of chlorothiazide. As of this time, we feel the use of enteric coated potassium chloride probably represents the drug of choice in place of ammonium chloride, as one can feel that chloride and potassium replacement will occur with a single medication.

Chlorothiazide was administered in divided doses ranging from 250 to 1,500 mg. per 24 hours, three to seven days a week. The average dose for long-term therapy was found to be 250 or 500 mg. given three times daily at roughly six-hour intervals. We observed that a greater diuretic response was obtained by giving chlorothiazide on a divided dosage schedule, two to three times a day, than by a single large dose in the morning and over three to four consecutive days each week. We observed that most patients could be kept at "dry" stable weights with three or four consecutive days of chlorothiazide administration; continuous daily administration did not seem necessary except in an occasional patient in whom control was more difficult.

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Read in the Symposium on the Newer Diuretics—Especially Chlorothiazide—Indications and Reported Use before the Section on General Practice at the 107th Annual Meeting of the American Medical Association, San Francisco, June 26, 1958.

Individual dosage adjustment was, of course, necessary, since all patients did not respond in a similar manner, some requiring as much as 1,500 mg. per day and others as little as 250 mg. one day a week. The usual initial dose was 250 mg. given three times a day for three or four consecutive days a week. Larger doses gave no greater diuresis than smaller effective doses, and we felt, further, that it was important to use the smallest possible effective dose for long-continued therapy. Subsequent dosage was determined by diuretic response and further need of therapy. There was no evidence of the loss of effectiveness of chlorothiazide in the presence of ammonium chloride acidosis.[5]

The onset of diuresis was more gradual than with a parenterally given mercurial agent, but continued in a more sustained and less vigorous manner, so that practically all patients agreed it did not cause them the same degree of muscular discomfort and marked frequency of urination, with the consequent frequent loss of sleep, seen with the shorter and more violent action of a parenterally given mercurial diuretic.

Results

Group 1 consisted of patients seen for the first time in congestive failure in whom chlorothiazide was administered in lieu of a mercurial diuretic. There were five patients in this group, three with arteriosclerotic heart disease, one with hypertensive cardiovascular disease, and one with rheumatic heart disease.

The average dosage of chlorothiazide was 250 mg. given three times a day for three days. The average weight loss was 6 lb. (2.7 kg.) at the end of a three-day period.

In group 2 were included patients in chronic congestive heart failure who required only occasional mercurial injections or were taking, orally, mercurial or nonmercurial diuretics. There were 25 patients, 9 with arteriosclerotic heart disease, 3 with hypertensive cardiovascular disease, and 13 with rheumatic heart disease.

Follow-up studies were done for periods of six weeks to four months, with an average of two and one-half months. The average dosage of chlorothiazide was 250 to 500 mg. given three times a day for three consecutive days each week. One patient received as little as 125-250 mg. one day a week. The average weight loss was 5 lb. (2.3 kg.). The usual loss was 3-8 lb. (1.3-3.6 kg.) at the end of each course.

No patient failed to be controlled as well as with mercurials given by oral or parenteral route or with orally given nonmercurials combined with mercurial agents. Three patients were improved much more than with the mercurial program. Two patients who had regularly received nonmercurial, orally given diuretics and, occasionally, mercaptomerin promptly lost 5-8 lb. when placed on chlorothiazide therapy. One patient who had been on therapy with an orally given mercurial agent lost 5 lb. in four days after use of chlorothiazide.

Group 3 included patients in chronic congestive heart failure who required regular injections of mercurial agents. There were 17 patients in this group, 11 with arteriosclerotic heart disease, 1 with hypertensive cardiovascular disease, and 5 with rheumatic heart disease.

Follow-up studies were done over periods of two to five months. The average dosage was 250 mg. given three times daily to 500 mg. given twice or three times daily for three consecutive days each week. Previous diuretic therapy had been with mercaptomerin alone or in combinations with chlormerodrin or nonmercurial, orally given diuretics. The average frequency of administration of mercurials by the parenteral route was every 7 to 14 days. After chlorothiazide therapy was begun, the average weight loss was 6 lb. and one patient lost 12 lb. (5.4 kg.).

No failures in treatment occurred. Every patient was as well controlled as, and a great deal more smoothly than, with the previous diuretic schedule.

In group 4 were patients in a refractory state of congestive failure in whom regular mercurials did not produce satisfactory results. There were three such patients, all with arteriosclerotic heart disease. All were unimproved on the mercurial program, and all were unimproved on chlorothiazide therapy. One patient noted some improvement after a return to mercurial therapy.

Report of Cases

Case 1 (group 1).—A 50-year-old man was admitted to the Henry Ford Hospital in congestive failure from arteriosclerotic and hypertensive heart disease. He had been on therapy with digitoxin, 0.2 mg. per day, and a low-salt diet. After admission, with no change in therapy, his weight remained stable for three days. On the morning of the fourth day, therapy with 500 mg. of chlorothiazide given twice daily was begun. At the end of two days, he had lost 7 lb. (3.2 kg.) in weight and all signs of congestive heart failure had cleared except for questionable minimal hepatic enlargement. He was continued on chlorothiazide therapy for three more days, with a further loss of 1 lb. (0.5 kg.) in weight. Serum sodium, potassium, chloride, and carbon dioxide levels were determined at this time, and all were within normal limits. He was then parenterally given 2 cc. of a mercurial to see if any further diuresis could be obtained. There was no change in weight or physical findings.

He was discharged to the outpatient department on maintenance therapy with digitoxin and a 1-Gm. salt diet, and follow-up examinations were done at about monthly intervals, with the requirement of parenterally given mercurials. After three months he showed evidence of increasing congestive failure. Chlorothiazide therapy was begun again, 250 mg. given three times daily three days a week, and ammonium chloride, 1 Gm. given four times daily the other four days of the week. Within 48 hours of institution of chlorothiazide therapy, he lost 4 lb. (1.8 kg.) in weight and his failure cleared. He has remained out of failure on this program for three months and has required no subsequent therapy with mercurial agents.

Case 2 (group 2).—A 44-year-old woman with rheumatic heart disease, auricular fibrillation, and chronic congestive failure had been on therapy with digitoxin, ammonium chloride, a 1-Gm. salt diet, chlormerodrin given five days a week, and, occasionally a parenterally given mercurial. When chlorothiazide therapy was begun, 250 mg. given three times a day three days a week, with 4 Gm. of ammonium chloride the other four days of the week, she lost 5 lb. in weight within four days. Symptoms were relieved, and she has maintained her improvement for more than two months with no need for chlormerodrin or any parenterally given mercurial agent.

CASE 3 (group 3).—A 70-year-old woman, treated at the Henry Ford Hospital for many years, had hypertensive cardiovascular disease, auricular fibrillation, and chronic congestive failure. She had been on therapy with gitalin, 0.5 mg. per day, a 1-Gm. salt diet, and rauwolfia (Raudixin), 100 mg. twice daily, and for many months had required parenteral injections of mercurial agents every 7-10 days with ammonium chloride given intermittently. Even on this program she had congestive failure periodically, with orthopnea, paroxysmal nocturnal dyspnea, and edema, usually beginning a few days prior to each injection of the mercurial. Chlorothiazide therapy was begun, 250 mg. given three times a day, three days a week and ammonium chloride the other four days of the week. On this program, she did not need any mercurial diuretic for five months and has had no orthopnea, paroxysmal nocturnal dyspnea, or edema for the first time in two or three years. It may be added that for 13 months the same continued satisfactory response has been seen.

CASE 4 (group 4).—A 65-year-old man had chronic, severe, intractable congestive failure and auricular fibrillation on an arteriosclerotic basis. He had been on therapy with digitoxin, 0.625 mg. daily, a 1-Gm. salt diet, intermittently given ammonium chloride and parenterally given mercurials, and, in the past, chlormerodrin and acetazolamide. The condition had not been well controlled with any of these programs. Recently, he had become almost completely resistant to even parenterally given mercurials. Therapy was begun with 500 mg. of chlorothiazide given twice daily three days a week, with ammonium chloride given intermittently, without response. Dosage was increased finally to 500 mg. given three times a day every day, but still this produced no satisfactory response. To this program was added parenterally given mercurials, 2 cc. every three to seven days, but with only minimal improvement—that is, a weight loss of 3 to 4 lb. with each injection. However, he would regain this weight within 24 to 72 hours. In summary, it was felt that chlorothiazide was of no significant benefit to this patient.

Toxicity

Our studies to date indicate chlorothiazide has little or no toxicity; however, as with all new drugs, alertness for signs of toxicity must be maintained. Its greatest potential danger seems to be the possibility of producing hypochloremia, hypopotassemia, or low sodium level syndromes, exactly as with mercurials. No serious electrolyte imbalance occurred in this study.

Patients with kidney disease and those with liver function impairment should be watched closely. The drug is apparently primarily excreted by the kidney, being eliminated completely within 24 to 48 hours.[4] However, in dogs subjected to nephrectomy and given chlorothiazide, considerable quantities could be recovered from the biliary tract.[3a]

Nausea or vomiting did not occur in any of our patients, the drug being exceedingly well tolerated. No neurological symptoms, such as headache, paresthesias, or peripheral neuritis, were found. Skin eruptions were not encountered; hemorrhagic and renal disturbances were checked for but not present.[4] In short, no evidence of serious toxicity was discovered in any of the patients treated in this report. However, since the completion of the report, and in the additional six months of use of the drug, three cases of skin rash have been observed. One of these was a true morbilliform type of rash, similar to that seen with the use of sulfonamides. The other two were very fine macular rashes, erythematous in nature, promptly subsiding with discontinuance of therapy. In one case, the drug was readministered in a smaller dose without return of the rash. Since the drug is a compound related to the sulfonamides, this type of rash may be found in some patients. The exact incidence is not definitely known but probably is well under 2%.

We would like to state that it is advisable to respect the potential danger of this drug, as with the mercurials, in treatment of patients with salt depletion and to be cautious in using it without the replacement of chlorides and potassium by means of ammonium chloride or potassium chloride where the latter can be safely administered. In those cases in which sodium or potassium depletion may occur, as in serious liver disease or in the long-continued use of steroid therapy, hypopotassemia may occur earlier than is the usual case, since the cation of excretion with chlorothiazide is chiefly sodium and, where this is not present, the next available cation, potassium, will be excreted in fairly large quantities. In patients who are digitalized, this hypopotassemia may potentiate the digitalis effect, resulting in digitalis intoxication and its subsequent manifestations.

Comment

Chlorothiazide appears to represent a significant advance in the diuretic management of patients with congestive heart failure, approaching the effectiveness of parenterally administered mercurials; its decided advantages are (1) effective oral administration, (2) apparent lack of toxicity, (3) high patient acceptance, (4) sustained diuretic action over prolonged periods of use (months) without apparent development of tolerance to the drug, without necessity of increasing dosage, and, therefor, with more even control of failure than seen with intermittent parenterally administered mercurials, and (5) fairly rapid onset and peak of action.

Summary

Chlorothiazide (6-chloro-7-sulfamyl-1,2,4-benzothiadiazine-1,1-dioxide) was found to be an extremely effective, orally given, nonmercurial diuretic agent resembling most closely, pharmacologically, the mercurial diuretics. Therapeutic dosage varied from 250 to 1,500 mg. given daily with apparent increased effectiveness on a divided-dose schedule. The usual maintenance dose was 500 to 1,000 mg. given three to four consecutive days of each week, alternating with ammonium chloride for its antihypochloremic-alkalosis effect, or the concurrent use of postassium chloride, 600 mg. given four times daily to protect from hypochloremia and hypopotassemia.

Its effectiveness was not diminished with constant administration, even over a period of several months. Chlorothiazide was found to be an effective replacement for regular orally or parenterally given mercurial agents and resulted in a smoother control of failure than that seen with intermittently, parenterally given mercurials in the majority of cases. It was also effective in short-term diuretic action (one to three days). In our limited experience, it was of no value in intractable, mercurial-resistant cases.

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The chlorothiazide used in this study was supplied as Diuril by the Merck, Sharp & Dohme Research Laboratories, Division of Merck & Co., Inc., Philadelphia.

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CHLOROTHIAZIDE AND PREMENSTRUAL TENSION

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The principal complaints of premenstrual tension noted a week prior to menses are nervousness, tension, swelling, headaches, depression, and breast soreness and turgidity; in severe form, these symptoms may progress to antisocial behavior and psychosexual abnormalities. Symptoms of the premenstrual tension syndrome may be due to latent edema, since many of the patients without apparent swelling were benefited by use of the diuretics alone. The usefulness of diuretics for control of premenstrual tension is well established. Chlorothiazide, in doses of 500 to 1,000 mg. administered daily for 7 to 10 days before menses, was given to 50 women with complaints referable to the premenstrual tension syndrome. Of the 50 patients, 33 complained of swelling. All of these patients showed an excellent response to chlorothiazide, with complete relief from their edema. Breast tenderness was a problem for eight patients, and, in each instance, the tenderness was relieved by chlorothiazide therapy. Headache was a presenting symptom in four patients, two of whom were relieved and two of whom noted no change while on chlorothiazide therapy.

Diuretics have been used with some success in control of the premenstrual tension syndrome. This study shows that chlorothiazide is particularly useful in controlling the edema and breast swelling often associated with premenstrual tension and, to a lesser degree, the tension itself.

The premenstrual tension syndrome is composed of many symptoms, any or all of which may be found in an individual patient. Most women note some changes the week before their menses, usually insufficient to require medical attention. The principal complaints noted at that time are nervousness, tension, swelling, headaches, depression, and breast soreness and turgidity; in severe form, these symptoms may progress to antisocial behavior and psychosexual abnormalities. During the premenstruum, some women exhibit nymphomaniacal tendencies, while others may have complete revulsion for the sex act. They often engage in domestic quarrels and become so distracted and distraught that their work efficiency is considerably lessened. This condition is of great importance to industries in which large numbers of women are employed, since efficiency drops, use of sick leave increases, and worker productivity is decreased.

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The etiology of premenstrual tension is still not clear. Many theories have been advanced: menstrual toxins,[1] excessive circulating estrogens,[2] deficient progesterone production,[3] excessive antidiuretic hormone,[4] allergy to the ovarian hormones, hypoglycemia,[5] and vitamin B deficiency.[6] Since the symptoms are so variable in kind and intensity, the only major hypothesis which can explain the syndrome is a dysfunction of the hypothalamic control of the autonomic nervous system.[7] What might be responsible for this dysfunction remains to be solved.

Nevertheless, premenstrual tension is an important and ever-present complaint for which relief is sought. Many different types of medicaments have been advocated for this syndrome: B-complex vitamins to enhance estrogen metabolism by the liver, estrogens to prevent ovulation, progestational substances to supplement endogenous progesterone, sedatives to combat the nervousness, testosterone to antagonize endogenous estrogen, and diuretics to prevent excess salt and water retention, to name a few. All of these have their adherents and are helpful in some cases. At present, the most widely used agents for control of premenstrual tension are the diuretics.

The usefulness of diuretics for control of premenstrual tension is well established. When edema is apparent as one of the major symptoms during the premenstruum, diuretics, used for 7 to 10 days before the onset of menses, are effective in preventing fluid accumulation. In some patients, the edema may be latent in character and swelling not be obvious; in them, control of salt and water excretion may be accompanied by gratifying relief from the other symptoms of the syndrome.

Until recently, the available diuretics were of three main types: those that increased glomerular filtration, such as caffeine; those that increased tubular urea excretion, such as ammonium chloride; and those that decreased tubular reabsorption of water by inhibition of carbonic anhydrase, such as acetazolamide. Adequate response with caffeine and ammonium chloride requires administration at frequent intervals throughout the day, causing some inconvenience to the patient and often resulting in missed doses and, thus, decreased effectiveness. The carbonic anhydrase inhibitors become less effective after four to five days' continuous use, necessitating an interrupted schedule of administration for optimum effect. Coincident with interruption of the schedule, swelling may occur and symptoms become troublesome until the diuretic therapy can be resumed.

Since the newer diuretic, chlorothiazide, can be given continuously without the development of resistance, it has been tried for control of premenstrual tension in 50 women.

Results with Chlorothiazide

Chlorothiazide, in doses of 500 to 1,000 mg. administered daily for 7 to 10 days before menses, was given to 50 women with complaints referable to the premenstrual tension syndrome. To evaluate the effectiveness of this diuretic, the syndrome was broken down into four symptoms and the patients were judged on their relief from each symptom: nervousness and tension, swelling, breast soreness, and headaches (see table). An individual patient might have any or all of these symptoms.

Severe nervousness and tension was a symptom in 42 patients, of whom 21 had satisfactory relief with chlorothiazide alone. Addition of a mild sedative or tranquilizer, such as the barbiturate vinbarbital (Delvinal), meprobamate (Equanil), or promazine (Sparine) hydrochloride, usually alleviated this symptom in the patients in whom chlorothiazide alone was not satisfactory.

Of the 50 patients, 33 complained of swelling. All of these patients showed an excellent response to chlorothiazide, with complete relief from their edema. Breast tenderness was a problem for eight patients, and, in each instance, the tenderness was relieved by chlorothiazide therapy. Headache was a presenting symptom in four patients, two of whom were relieved and two of whom noted no change while on chlorothiazide therapy.

Results of Chlorothiazide Administration in Fifty Patients with Premenstrual Tension

	Symptom							
	Tension		Swelling		Breast Soreness		Headache	
Daily Dose,* Mg.	Relieved, No.	Not Relieved, No.	Relieved, No.	Not Relieved, No.	Relieved, No.	Not Relieved, No.	Relieved, No.	Not Relieved, No.
500	6	11	12	0	4	0	0	0
1,000	15	10	21	0	4	0	2	2
Total	21	21	33	0	8	0	2	2

* Given 7-10 days before menses.

Comment

The premenstrual tension syndrome is of widespread importance, affecting most women to some extent. When it is sufficiently severe to require medical help, relief may be obtained from a great variety of therapeutic regimens.

Diuretics in some form have been used with moderate success for a long time in the treatment of this condition. Ammonium chloride, by increasing the urea excretion and altering the acidity of the urine, is one of the most popular diuretics and has met with variable degrees of success. With the advent of the newer diuretics, more uniform results have been obtained.

The major disadvantage of ammonium chloride is that its administration must be repeated at frequent intervals each day to attain an optimal response, causing considerable inconvenience to the patient and often resulting in missed or irregularly spaced doses. Acetazolamide and other carbonic anhydrase inhibitors maintain their peak effectiveness for only four to five days, after which some swelling may occur. Chlorothiazide, on the other hand, continues to be effective for a prolonged period of time without the development of tolerance.

In the series of patients reported here who complained of premenstrual tension, chlorothiazide, given in a dosage of 500 to 1,000 mg. daily for the last 7-10 days before menses, was uniformly successful in preventing peripheral edema and breast tenderness. The nervousness and tension was relieved in one-half of these patients, whereas the balance of the patients noted no improvement. However, combining the chlorothiazide with a mild *tranquilizer was effective in controlling the tension* of those patients who noted no relief from chlorothiazide alone.

Premenstrual headaches were relieved in two of four patients with this complaint by chlorothiazide alone. The other two required the addition of tranquilizers.

This study supports the view that the symptoms of the premenstrual tension syndrome may be due to latent edema, since many of the patients without apparent swelling were benefited by use of the diuretics alone. On the other hand, it supports the contention that an alteration in salt and water metabolism is not the primary problem in all patients with premenstrual tension, since relief of all apparent swelling had no effect on the tension, nervousness, and headaches of half the patients with these complaints. This serves to reemphasize the fact that no single regimen of treatment is successful in all cases of premenstrual tension; treatment must be individualized to the presenting symptoms.

Summary

A newer, orally given diuretic, chlorothiazide, has been utilized in the treatment of 50 women complaining of premenstrual tension in a dose of 500 to 1,000 mg. daily for 7 to 10 days before menses. The effectiveness of its use was assessed by analysis of the relief of four major complaints referable to this condition, any or all of which may have been present in an individual patient.

Chlorothiazide is an excellent agent for relief of swelling and breast soreness associated with the premenstrual tension syndrome, since all patients with these complaints were completely relieved.

Where tension, nervousness, and headaches are major factors, chlorothiazide may provide relief; *approximately half of the patients in this series* were benefited, the others noting no improvement. Mild sedatives or tranquilizers given along with chlorothiazide were helpful in resistant cases.

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The chlorothiazide used in this study was supplied as Diuril through Dr. John R. Beem of Merck, Sharp & Dohme, Division of Merck & Co., Inc., Philadelphia.

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TREATMENT OF CANCER.—Advances in the treatment of cancer have been made in all the major fields of therapy, but critical assessment of the results obtained indicates that there is little justification for complacency. Although much has been achieved in affording the patient good palliation and enabling him to live in comfort with the disease, the long-term survival or "cure" rates have shown little improvement. Perhaps the most significant advance has been the clinician's appreciation that larger operations and more complex and powerful therapy machines do not, of necessity, confer better treatment on the patient. Assessment of the differing biological potentials of each individual cancer has led to a more careful selection of the appropriate form of treatment. Surgeon, radiotherapist, and chemotherapist are appreciating that the future of cancer therapy lies at the cellular or intracellular level and are directing their efforts and attention accordingly.—A. G. Jessiman, F.R.C.S., and F. D. Moore, M.D., Advances in the Treatment of Cancer, *The Practitioner*, October, 1958.

MORPHOLOGY AND RACIAL DISTRIBUTION OF FATAL COCCIDIOIDOMYCOSIS

REPORT OF A TEN-YEAR AUTOPSY SERIES IN AN ENDEMIC AREA

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The generalization that dark-skinned ethnic groups are particularly susceptible to infectious granulomas was tested in a study of 4,989 autopsies performed during a 10-year period in an area where coccidioidomycosis and tuberculosis were both constantly present. Difficulties were encountered in classifying the subjects as to race and also in settling diagnostic questions in cases of arrested or inactive granulomatous lesions, but in persons who died with coccidioidomycosis it was always easy to demonstrate the organisms in the lesions. Acute forms of coccidioidomycosis, with massive suppuration and overwhelming dissemination, occurred in Negroes, Caucasians, and Mexicans; so did the subacute or chronic meningitic forms without obvious visceral involvement. There was evidence that all three groups were living in unfavorable environments. Nevertheless the incidence of fatal disease showed some striking differences. The incidence of fatal coccidioidomycosis was only slightly higher in Mexicans than in Caucasians, but that in Negroes was 10 times as high as in Caucasians. The incidence of fatal tuberculosis was only slightly higher in Negroes than in Caucasians, but in Mexicans it was very much higher. A group of Filipinos living in particularly bad circumstances appeared to be particularly vulnerable to both diseases. The supposed generalization, therefore, did not hold, and it is evidently important to specify which ethnic group and which infectious granuloma is concerned.

The meticulous study of Forbus and Bestebreurtje [1] and the admirable review by Fiese [2] suggest the desirability of further data on the morbid anatomy and race-sex distribution of fatal coccidioidomycosis. Observations on the histopathology of coccidioidomycosis have been presented elsewhere.[3] In view of the increasing national interest in the disease, it seemed appropriate to analyze an experience with fatal cases studied at autopsy in a civilian hospital in an endemic area with reference to morphology and race distribution. Data on fatal tuberculosis in the same autopsy population are presented for comparison and contrast.

Methods and Material

The Kern County General Hospital has 500 beds for acutely and 200 for chronically indigent sick persons of the southernmost county of the San Joaquin Valley. It is affiliated with the county tuberculosis sanitarium in a neighboring community. Figures for admissions for six years (July, 1951, to July, 1957) total 63,015–26,125 male and 36,890 female. A great many of the latter were admitted to the obstetric service. The figures by race are as follows: Caucasian, 40,163; Mexican, 11,958; Negro, 10,142; and others, 752. The conclusion as to race was based on the individual's statement plus data on parents and their place of birth. Mexican, I believe, can be defined as a person with a Spanish name with some Spanish blood but largely American Indian (Amerind) parentage, whether born in California, Texas, Arizona, New Mexico, or old Mexico. Unfortunately, the census statistics list most Mexicans as Caucasian, despite the importance of the Amerind strain.

The pathology laboratory of the hospital was under the direction of Dr. J. D. Kirshbaum from late 1946 to early 1949 and has been supervised by myself since April, 1950. From Jan. 1, 1947, to Dec. 31, 1956, 4,989 postmortem examinations were done. About one-third of these were done by request of the coroner on persons who died outside the hospital. However, many of these subjects had prior county hospital records, and most of them belonged to the indigent rather than the affluent class. Supplementary data on the race of these subjects were obtained from the police and the coroner when necessary.

Of the 4,989 subjects in the series, 3,383 were males and 1,606 females. The preponderance of males reflects the generally observed higher male mortality. In this area there is, perhaps, an unusual number of unattached males who take very poor care of themselves. Thus, for example, the Filipino colony at the northern end of the county is almost entirely male. Caucasian subjects numbered 3,558 (2,471 male and 1,087 female); Mexican, 629 (369 male and 260 female); Negro, 667 (431 male and 236 female); Filipino, 58 (all male); and other or unidentified races, 77 (54 male and 23 female).

Autopsy procedure has included microscopic study of any gross lesions and routine sections of major viscera even in the absence of gross lesions. Hotchkiss-McManus and acid-fast stains and cultures on Sabouraud's and Petragnini's mediums have been utilized freely.

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In none of the persons who died from coccidioidomycosis was there difficulty in demonstrating the organisms in the lesions. In a few with tuberculosis, antibiotic treatment insufficient to arrest the disease interfered with the demonstration of Mycobacterium tuberculosis post mortem. However, in all listed as having fatal tuberculosis, M. tuberculosis was demonstrated some time during the course of the disease; usually, it was found abundantly in tissue, at postmortem examination.

With arrested or inactive granulomatous lesions, the differential etiological diagnosis is frequently impossible. A solitary inactive subpleural granuloma showing spherules on wet mount or on section stained with hematoxylin-eosin or Hotchkiss-McManus stains can confidently be classed as coccidioidal, even though such lesions have not yielded viable organisms on culture.[2] A lesion of similar appearance but showing M. tuberculosis on section, smear, or culture can be classed as tuberculous. However, a great many such lesions show neither fungi nor M. tuberculosis. No attempt has been made, therefore, to compile figures for nonfatal tuberculosis, while those for nonfatal coccidioidomycosis are presented with emphasis on their incompleteness.

Table 1.—*Incidence of Fatal Coccidioidomycosis in Autopsy Series, 1947-1956*

	Meningitis, No.				Visceral Dissemination Without Meningitis, No.							Total Fatalities	
Population Group*	Lung Only	Without Psoas Abscess	With Psoas Abscess	Total	With Psoas Abscess	Without Psoas Abscess	Total	Visceral Dissemination with Meningitis Not Determined, No.	Fatal Dissemination, Total	Fatal Acute Pneumonitis, No.	Fatal Cavity, No.	No.	%
Caucasian													
Male (2,471)	2	7	...	9	...	...	...	1†	10	1	...	11	0.455
Female (1,087)	2	3	...	5	...	1	1	...	6	...	...	6	0.552
Mexican													
Male (369)	2	1	...	3	...	1	1	1	5	...	...	5	1.36
Negro													
Male (431)	1	7	2	10	3	8	11	2	23	...	...	23	5.34
Female (236)	1	5	1	7	...	3	3	...	10	1	1	12	5.08
Filipino													
Male (58)	1	1	1	3	...	1	1	...	4	...	...	4	6.90
Other													
Male (54)	1‡	1§	...	2	...	...	...	...	2	...	...	2	...
Total (4,989)	10	25	4	39	3	14	17	4†	60	2	1	63	1.26

* Numbers in parentheses refer to group totals from which fatality percentages are derived (there were 260 Mexican females and 23 "other" females without findings relating to coccidioidomycosis; there were no Filipino females in study).

† One with psoas abscess.

‡ Amerind.

§ Chinese.

Results

After careful review, 63 deaths were attributed to coccidioidomycosis. One was due to hemorrhage from a chronic cavity. A Negro woman who had refused surgery died at home. Cultures of sputum had shown coccidioides immitis, and postmortem cultures of tissue were likewise positive. Sections showed the organisms to be largely in the mycelian phase. Two deaths were due to acute suppurative coccidioidal pneumonitis without evident dissemination. In the remaining 60 patients the disease had spread beyond lungs, pleura, and thoracic lymph nodes, i. e., it was disseminated. Meningitis was demonstrated in 39 of these. However, it was the sole metapulmonary lesion in only 10. Twenty-nine showed meningitis plus visceral dissemination, and it may be well to emphasize that this, in my experience, has been the most common pattern of fatal coccidioidal disease. In 17 with fatal disseminated disease there was no meningitis and in 4 the meninges were not examined. Of the 60 subjects with disseminated disease, 8 had bulky psoas abscesses.

One important lesson was the fact that the antemortem diagnosis of fatal coccidioidomycosis is not infrequently missed, even in clinics in which a good deal of it is seen. Chronic coccidioidal meningitis and acute disseminated coccidioidomycosis with subcutaneous abscess or cutaneous granuloma are not often overlooked, but other forms may well be. Thus, the diagnosis was missed prior to autopsy in the two cases of acute pneumonitis without dissemination and in eight cases of disseminated disease. Coccidioidomycosis should, therefore, be suspected in any obscure febrile illness in a person who has been in an endemic area.

Of the 63 subjects, 11 were Caucasian male, 6 Caucasian female, 5 Mexican male, 23 Negro male, 12 Negro female, 4 Filipino male, and 2 other male (1 Chinese, 1 Amerind). Of the 17 subjects with disseminated disease without meningitis, who presumably died of the dissemination before they had time to get meningitis, 14 were Negro and 1 was Filipino. Of the eight with psoas abscess, one was a Caucasian male, one a Filipino, and the remainder Negroes (five male, one female). On the other hand, of the 10 with meningitis as the sole metapulmonary lesion, only 2 were Negro and 1 Filipino. Four were Caucasian. The data on fatal coccidioidomycosis are summarized in table 1.

Data on 71 cases in which nonfatal coccidioidomycosis could be diagnosed are given in table 2. As already mentioned, the true incidence of inactive pulmonary residuals is certainly much higher than these figures indicate. At present, no way is known to recognize such residuals as coccidioidal in the absence of stainable spherules. Some comment on the 10 cases listed as "nonfatal disseminated" may be appropriate. In two of these cases, the diagnosis had been established during life, but no definite traces of it could be found at autopsy. A middle-aged Negro woman had a retropharyngeal abscess which yielded C. immitis on culture. She died, three and one-half years after diagnosis, of a carcinoma of the cervix. At autopsy, a subpleural granuloma showed neither acid-fast bacilli nor spherules. No other possible or probable coccidioidal lesions could be found. A 1-year-old Mexican boy had pneumonitis in 1948, followed by numerous skin and bony abscesses full of C. immitis and a high complement-fixation titer. With treatment with a drug now believed of little value the lesions dried up. He died of sympathoblastoma with widespread metastases in 1952, and no coccidioidal residuals could be found at autopsy. Clearly, therefore, a person who has serious coccidioidal disease will not necessarily die of it. In six patients the metapulmonary lesions were few and apparently inactive. In two subjects the process might well have proved fatal if something else had not intervened first. In one of these (a Filipino male) the actual cause of death appeared to be chronic glomerulonephritis, while in the other (a Caucasian male) it was coronary artery disease.

TABLE 2.—*Incidence of Nonfatal Coccidioidomycosis in Autopsy Series, 1947-1956*

Population Group*	Inactive Pulmonary Disease, No.	Pneumonitis, No.	Cavitation, No.	Dissemination, No.	Total No.	Total %
Caucasian						
Male (2,471)	23	2	1	5	31	1.25
Female (1,087)	13	...	1	...	14	1.29
Mexican						
Male (369)	...	1	...	1	2	0.542
Female (260)	2	...	...	...	2	0.769
Negro						
Male (431)	12	...	...	1	13	3.02
Female (236)	4	...	2	1	7	2.97
Filipino						
Male (58)	...	...	...	2	2	3.45
Total (4,989)	54	3	4	10	71	1.62

* Numbers in parentheses refer to group totals, from which disease total percentages are derived (there were 77 in the "Other" category without findings relating to nonfatal coccidioidomycosis; there were no Filipino females in study).

In this series of 4,989 autopsies, there are 99 cases in which, on review, death is attributed to tuberculosis (table 3). Unfortunately, many of these autopsies were not done with the enthusiastic thoroughness which characterized those done to determine coccidioidomycosis. Thus, in too many instances the meninges were not examined. The disease appeared restricted to the lungs in 30, while there was evidence of dissemination in 69. Twenty-nine of the subjects were Caucasian male, 12 Caucasian female, 18 Mexican male, 23 Mexican female, 11 Negro male, 2 Negro female, 3 Filipino male, and 1 Amerind male. The disease appeared localized in 15 of the Caucasian males and 5 of the Negro males. Localized disease was relatively less frequent in the other groups.

TABLE 3.—*Incidence of Fatal Tuberculosis in Autopsy Series, 1947-1956*

	Location		Total Fatalities	
Population Group*	Disseminated, No.	Localized Pulmonary, No.	No.	%
Caucasian				
Male (2,471)	14	15	29	1.17
Female (1,087)	8	4	12	1.10
Mexican				
Male (369)	16	2	18	4.88
Female (260)	19	4	23	8.85
Negro				
Male (431)	6	5	11	2.55
Female (236)	2	...	2	0.849
Filipino				
Male (58)	3	...	3	5.17
Other				
Male (54)	1†	...	1	...
Total (4,989)	69	30	99	1.98

* Numbers in parentheses refer to group totals, from which fatality percentages are derived (there were 23 "Other" females without findings relating to coccidioidomycosis; there were no Filipino females in study).

† Amerind.

Comparative racial incidence of fatal coccidioidomycosis and fatal tuberculosis is given in table 4. It will be noted that the Filipinos appear decidedly vulnerable to both diseases and that coccidioidal deaths were much more frequent than tuberculous deaths in the Negroes, while tuberculous deaths were the more numerous in the Caucasians and the Mexicans.

TABLE 4.—*Comparison, by Race, of Incidence of Fatal Coccidioidomycosis and Fatal Tuberculosis in Autopsy Series, 1947-1956*

		Fatal Coccidioidomycosis		Fatal Tuberculosis		
Population Group	Total in Group	No.	%	No.	%	Ratio (%)
Caucasian						
Male	2,471	11	0.455	29	1.17	38.0
Female	1,087	6	0.552	12	1.01	50.0
Mexican						
Male	369	5	1.36	18	4.88	27.8
Female	260	...	...	23	8.85	...
Negro						
Male	431	23	5.34	11	2.55	209.0
Female	236	12	5.08	2	0.849	600.0
Filipino						
Male	58	4	6.90	3	5.17	133.0
Other (male)	54	2*	3.70	1†	1.85	...
Series Total	4,989	63	1.26	99	1.98	63.6

* 1 Amerind; 1 Chinese.

† Amerind.

Comment

Under the leadership of Drs. Claude Babcock, Bert Cotton, Ralph Cunningham, George Paulsen, and others, this community has kept pace with

Dr. Robert Bellg Library

modern methods for detection and medical and surgical treatment of tuberculosis. The county is rightly considered a hyperendemic area for coccidioidomycosis. It is of some interest, therefore, that in this autopsy series the fatalities due to tuberculosis exceeded those due to coccidioidomycosis. There was definitely less enthusiasm in requesting consent for autopsy in cases of known tuberculosis than in those of known coccidioidomycosis. Probably, therefore, the actual difference in fatality between the two diseases is even greater than these figures indicate.

The apparent vulnerability of the small Filipino group to both diseases may perhaps be attributed in part to their exceedingly unfavorable environment. However, it is doubtful whether the Caucasian, Mexican, and Negro populations represented in this autopsy series differ markedly in nutrition, domestic crowding, and exposure to agricultural dust. The differences in incidence of fatal coccidioidomycosis and fatal tuberculosis, and in the ratio between the two, among these three groups are, therefore, of considerable interest.

It will be noted that the incidence of fatal tuberculosis among the Negro females was of the same order as that among Caucasian males and females, while the incidence among Negro males was a little higher. The difference in incidence between Negro males and Caucasian males is slightly less than twice its standard deviation and, hence, probably not significant. The difference between the total Caucasian and Negro fatal tuberculosis rate is likewise between 1 and 2σ. Since larger statistical surveys [4] from other areas have established a significantly higher tuberculosis death rate in Negroes than in Caucasians, these figures may reflect merely the smallness of the samples and the decidedly underprivileged status of the Caucasian group. However, the incidence of fatal coccidioidomycosis in Negroes in this series appears about 10 times that of Caucasians; these differences are outstandingly significant. Conversely, the difference in incidence of fatal coccidioidomycosis between Caucasian and Mexican males is probably not significant, while the difference between all Caucasians and all Mexicans in this respect is less than 1σ. Yet, there is four times as much fatal tuberculosis in Mexican as in Caucasian males and eight times as much in Mexican as in Caucasian females, and, here again, the differences are statistically significant. Current figures on admissions to the county tuberculosis sanitarium corroborate the belief that in this area tuberculosis is conspicuously a Mexican disease. Finally, direct comparison between the Negro and Mexican groups, small though the numbers are, shows fatal tuberculosis to be significantly more common in the Mexicans and fatal coccidioidomycosis significantly more common in the Negroes.

With regard to the types of fatal coccidioidal disease seen in Caucasians, Mexicans, and Negroes, it will be noted (table 1) that, while massive suppuration, as represented by psoas abscess, and overwhelming dissemination ending fatally before meningitis can develop both occur in all three races, they are more common in the Negro than in the Caucasian or Mexican. Conversely, subacute or chronic meningitis without obvious visceral dissemination was noted twice in Negroes, twice in Mexicans, and four times in Caucasians.

It is suggested, therefore, that generalizations such as "the dark-skinned races are particularly susceptible to infectious granulomas" may be of very limited usefulness. At least in speaking of Mexicans and Negroes, in regard to coccidioidomycosis and tuberculosis, it seems important to specify which race and which infectious granuloma.

Summary

In a study of a 10-year autopsy series, comprising 4,989 autopsies, in a hyperendemic area of coccidioidomycosis, there were 99 fatalities attributable to tuberculosis as compared with 63 to coccidioidomycosis. The incidence of fatal tuberculosis was only slightly higher in Negro subjects than in Caucasian, but the incidence of fatal coccidioidomycosis in the Negroes was about 10 times that in Caucasians. Conversely, the incidence for Mexicans of fatal coccidioidomycosis was only slightly higher than that of the Caucasians, while that of fatal tuberculosis was very much higher. Filipinos appeared particularly vulnerable to both diseases. Fulminating dissemination of coccidioidomycosis and massive suppuration, although it occurred in Caucasians and Mexicans, was much commoner among Negroes.

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SYMPTOMATIC HIATUS HERNIA

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Herniations through the esophageal hiatus of the diaphragm often give rise to elusive symptoms that are common to many other abdominal disorders; they sometimes also lead to peptic esophagitis, severe hemorrhages, and strictures. The authors recommend that medical management be tried first but that operation be performed if such management fails to relieve symptoms. Of 65 patients who underwent surgery for symptomatic hiatus hernia, 45 had complained of pain that was poorly localized but commonly described as a sensation of fulness, bloating, or pressure. Esophagoscopy was carried out in 48 patients, and the findings were reported normal in 22. Surgical repair can be done by either the thoracic or the abdominal route. The essential aim is to bring the gastroesophageal junction back into position below the diaphragm and to keep it there. The hernial sac must be destroyed without injury to the sphincteral mechanism about the cardia. This depends upon a thorough understanding of the functions of the crura of the diaphragm, the muscularis mucosae and muscularis externa of the stomach, various parts of the endoabdominal fascia, and the left gastric artery in maintaining the usual position of the cardia. Close attention to detail is mandatory. The patients of this series were followed for periods of time from six months to seven years, and 59 of the 65 became and remained free from symptoms after operation.

Most patients with symptomatic hiatus hernia can exist indefinitely on a medical regimen if the physician and patient are satisfied with a chronic state of semi-invalidism.[1] After moderate symptoms have become established, it is rare that cure will result without surgical treatment. Herniation of the cardia through the hiatus causes loss of integrity of the cardioesophageal valve, allowing reflux of gastric juice into the lower part of the esophagus. The repeated insults of the acid-pepsin with resultant escharotic action cause permanent damage and eventual destruction of the enigmatic one-way valve. Medical treatment may suppress the symptoms by neutralizing gastric acid; however, the treatment schedule must be rigidly followed. Many patients will not adhere to a strict program, and the peptic esophagitis progresses. The vulnerable mucous membrane and muscularis mucosae of the lower part of the esophagus are eventually destroyed, resulting in stricture with chronic dysphagia, pyrosis, and malnutrition.

The increasing awareness of hiatus hernia as a cause for bizarre and elusive symptoms is interesting, with the number of operations performed for this disease increasing markedly in recent years. Analysis by year for this hospital reveals 9 operations in 1950, 3 in 1951, 2 in 1952, 5 in 1953, 5 in 1954, 17 in 1955, 11 in 1956, and 13 in 1957 (total, 65). It is still curious, however, to note how many doctors refuse to accept hiatus hernia as a cause for symptoms. The skeptics would soon revise their opinions if they had under their care miserable patients with esophageal strictures secondary to the peptic esophagitis of hiatus hernia.

Materials

This is a report of 71 patients who received surgical treatment for symptomatic diaphragmatic hernia at the Wadsworth General Hospital between 1950 and 1957. Types of hernia included sliding (61), paraesophageal (4), traumatic (4), pleuroperitoneal (1), and congenital short esophagus (1). The youngest patient was 23 years old and the oldest 72 years, with a mean of 55.6 years. Of the 65 patients with symptomatic hiatus hernia, 22 were in the 50-to-59 age group, 25 in the 60-to-69 group, and 4 over 70 years of age. Fourteen patients were below 50 years of age, with 2 in the 20-to-29 group, 3 in the 30-to-39 group, and 9 in the 40-to-49 group.

Diagnosis

The symptoms are not specific and are common to many disorders of the upper part of the abdomen and angina pectoris. Pain was the most constant symptom, occurring in 45 (68.2%) cases, and consisted of a sensation of fulness, bloating, pain radiating to back, postprandial recumbency pain usually in the epigastrium, and pressure symptoms. Pyrosis and vomiting each occurred 25 (37.9%) times, and dysphagia occurred in 22 (33.3%) cases. Bleeding occurred in 21 (32.3%); in nine patients the bleeding was severe, and one required four transfusions in another hospital. It would have been

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our practice to repair this hernia as soon as the patient had had adequate blood replacement. This patient eventually required an operation.

In 51 patients the duration of symptoms was less than six years, and in 28 of these it was less than two years. The remaining 15 had symptoms ranging up to 32 years' duration.

In all but one patient the diagnosis was established preoperatively by roentgenograms. In this one patient the hernia was discovered incidentally during a gastrectomy for ulcer disease and was repaired concomitantly.

Esophagoscopy was performed in only 48 cases, but it is now our firm belief that all patients with symptomatic hiatus hernia should have esophagoscopy performed prior to surgery. Esophagoscopic examination will enable the surgeon to accurately evaluate the lower part of the esophagus for evidence of esophagitis, ulceration, and stricture. Severe inflammatory changes may persist for prolonged periods after surgery, and in some cases the patient will have delayed too long in seeking aid and irreversible changes will have taken place.

Findings in 48 patients (72.7% of the total group) who had esophagoscopy were as follows: In 22 (45.8%) results were reported as normal. Twenty-one (43.8%) had esophagitis, three (14.3%) with ulceration, two (9.5%) with stricture, and one (4.8%) with associated ulceration and stricture. Esophageal stricture with normal mucosa above it was present in three patients (6.3%). The latter represents nature's attempt to protect the mucosa above the level of the stenosis from the corrosive action of gastric juices, but it does not improve the comfort and nutrition of the patient. Congenital short esophagus was reported on two occasions (4.2%); however, at surgery only one of these proved to be a true congenital lesion, the other representing a high cardioesophageal junction from recoil elastic shortening of the esophagus.

In addition to evaluating esophagitis, esophagoscopy is of value in eliminating the presence of a neoplasm in the hernia not diagnosed by the x-ray studies. We have not seen malignant tumors associated with hiatus hernias; however, Robb[2] reported three cases, and Grimes and Stephens[3] two. The combination of hiatus hernia and malignant tumor is admittedly rare, but knowledge of its existence prior to surgery would minimize the importance of the hernia in favor of the neoplasm and thus change the operation performed.

Associated diseases in the upper part of the abdomen and angina may be misleading, and in many patients errors in diagnosis have been made prior to discovery of the true cause of symptoms. Harrington[4] states that an average of three erroneous diagnoses were made in each of his cases; he lists them as cholecystitis, peptic ulcer, hyperacidity, secondary anemia, heart disease, carcinoma of the cardia, stricture, intestinal obstruction, appendicitis, and thoracic tumor. We have encountered similar situations, and where two diseases occur simultaneously the problem of distinguishing which disease is causing the symptoms sometimes presents a problem. We have used diagnostic pneumoperitoneum[5] a few times to help identify the symptomatic process and are encouraged by its results in difficult diagnostic problems. Induction of pneumoperitoneum apparently causes reduction of the hernia when the patient is in the upright position, and if symptoms are due to the hernia they will be relieved. When the patient is in the supine position, herniation again occurs and symptoms reappear.

Of the 65 patients 21 (32.3%) had peptic ulcers, and we feel there is a strong association between these two conditions, with the common denominator being gastric hyperacidity. Of the 21 patients who had esophagitis, 12 also had gastric or duodenal ulcer. It is now our custom to obtain studies for gastric acidity, and in many this level is high.

Burford and Lischer[6] advised use of Finney pyloroplasty alone in treatment of hiatus hernia with simple esophagitis, the concept being that pyloroplasty assures downward outflow of gastric acid pepsin, thus preventing reflux by decreasing resistance at the pylorus. With high gastric acidity or with peptic ulcer, associated with hiatus hernia, a more satisfactory procedure would be repair of the hernia and performance of vagotomy and pyloroplasty.

Esophageal acid reflux studies and Bernstein's test[7] are helpful in difficult problems. In the latter test, a small plastic tube is passed into the distal part of the esophagus and either dilute hydrochloric acid or saline solution is dripped through the tube. When esophagitis is present, the dilute acid will cause reduplication of the symptoms as it reaches the distal part of the esophagus but the saline solution will not. This test is more accurate in assessing mild degrees of esophagitis than is esophagoscopy, since the earliest changes are submucosal and not mucosal and, therefore, not visible to the naked eye.

Previous Treatment

Forty-three patients had received nonsurgical treatment, and 24 (48%) had been under apparently adequate medical management for a period ranging from several months to 11 years. The evaluation of prior medical treatment from the patient's history is sometimes difficult, but under adequate treatment we included those who stated they had been under prolonged care directed by a physician, clinic, or hospital. It should again be emphasized that many persons will not follow the ideal treatment program so necessary to control the regurgitant esophagitis. Seven patients (14%) had had one or more previous operations directed at repair of the hernia; they represented a special challenge, since such hernias have a higher recurrence rate than those in patients not previously operated on. Sixteen (24.2%) had received no prior treatment.

Operation

Most of the operations were performed by residents in general and thoracic surgery, with variations in technique being utilized. The basic principles of repair can be accomplished through either abdomen or chest, and these principles should not be compromised, whichever route is used. When associated abdominal disease is present the abdominal approach may be preferable, in that treatment of both lesions can be done simultaneously. In some patients exposure through the abdomen is so difficult that it becomes a tedious and almost impossible operation. The transthoracic approach, in our hands, has been more satisfactory, and even the cases which would appear most trying are reduced to technically easy operations. The periesophageal inflammatory adhesions and fibrosis can be properly managed under direct view through the chest approach.

The most important factor in repair of hiatus hernia is to reduce the gastroesophageal junction below the diaphragm and maintain it there. If the phrenoesophageal ligament is of sufficient strength, it should be sutured to the abdominal surface of the diaphragm; however, frequently this ligament is a tenuous, almost ethereal membrane of little value. The crura should be approximated posteriorly, since anterior approximation changes the normal relationships between the esophagus and the crus, with backward displacement from its normal position, and leaves open the weak, unprotected area posteriorly. The hernia sac must be destroyed and the pinchcock mechanism kept intact by avoidance of injury to the cardia, crura, and oblique angle of the esophageal entrance into the stomach.

Results

Of the 65 patients who were operated on, 59 (90.8%) have been asymptomatic over a follow-up period ranging from six months to seven years. This compares favorably with other reported series.[3] In five (7.7%) results are classified as failures because of persistent symptoms; however, three of these patients complain only of "gas." One has a recurrent stricture, and one had severe esophagitis when last seen.

One patient died on the fourth postoperative day of a massive pulmonary atelectasis, and autopsy revealed an unrecognized, clear-cell carcinoma of the kidney and cirrhosis of the liver. This one death represents a mortality of 1.5%.

There were five (7.7%) complications of surgery, one of which was a nosocomial staphylococcic pericarditis which has cleared on antibiotic treatment (10-month follow-up). One patient had postoperative partial gastric volvulus with pyloric obstruction and recovered after a subtotal gastrectomy was done. Two have chest wall pain which is severe and persistent, and one had persistent esophageal stenosis eventually treated by esophagogastrectomy. Of the patients with complications, none have, at the time of writing, hiatus hernia symptoms and in two the complications cleared with further treatment.

Forty-four (67.7%) of the 65 patients were studied postoperatively with x-rays, and 7 (10.8%) had a small recurrence of the hernia. All but one were asymptomatic, and in this one case symptoms were controlled by medical management.

Comment

The gullet traverses the posterior mediastinum from the hypopharynx to the abdomen and passes through the hiatus. Its normal elastic recoil action pulls it upward against the forces which tend to maintain the normal anatomic relationships. The right and left diaphragmatic crura arise from the bodies of the first three or four lumbar vertebrae. The left fans out onto the diaphragm and does not contribute to the hiatus. The hiatus (fig. 1*A*) is formed entirely from the right crus as a teardrop-shaped split in the muscle fibers.[8] The right crus originates on the vertebral bodies, arcs up anteriorly along the gentle curvature of the diaphragm, passes around the esophagus to the left, and passes downward posteriorly toward the right where it meets its ascending limb. In the posterior area behind the esophagogastric junction is a fat pad which is unsupported and unprotected. In the supradiaphragmatic region this represents the posterior mediastinum, and the herniated stomach passes in this direction and upward. Herniation of the bare area

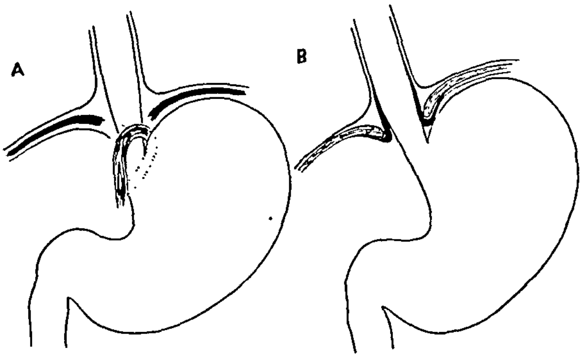

Fig. 1.—*A*, hiatus shown from anterior aspect illustrating formation of hiatus by right crus of diaphragm. *B*, phrenoesophageal ligament shown from anterior aspect. Heavy black lines illustrate ligament as continuation of endoabdominal fascia up through hiatus and insertion onto esophagus.

of the stomach and esophagogastric junction is comparable to a sliding hernia of the sigmoid colon, and reduction at surgery is accomplished in the same manner.

The endoabdominal fascia is a continuum and, in different areas, bears different names. In the lower part of the abdomen it is called the transversalis fascia; however, at the diaphragmatic hiatus region it is called the diaphragmatoesophageal fascia or phrenoesophageal ligament.[9] It ascends through the hiatus and, 1 or 2 cm. above the esophagogastric junction, inserts onto the esophagus and helps maintain the normal relationship of the esophagogastric junction to the diaphragm (fig. 1*B*). The peritoneum is loose and is generally not considered to have any effect in this regard. The ligament is resilient and allows considerable play of the esophagus through the hiatus.

According to Barrett,[10] the left gastric artery plays the most important role in maintaining the usual position. It tethers the upper lesser curvature aspect of the stomach to the posterior abdominal wall and helps resist herniation; however, if stretched it will allow the cardia to slip into the mediastinum.

The intrinsic muscular sling of the stomach is a band of gastric muscularis which passes from the lesser curvature posteriorly around the esophagogastric junction to the anterior aspect of the stomach and assists the hiatal sling in maintaining the acute oblique angle of entrance of the esophagus into the right side of the stomach.[10] Loss of the acute angle, such as with depression of the fundus of the stomach by the tonic contraction of the diaphragm during vomiting, causes incompetence of the cardia.

The exact mechanism of action of the one-way valve is not known; however, the oblique angle of entrance of the esophagus into the stomach is felt to be very important. Increased intragastric pressure tends to assist the valve mechanism having normal relationships by closing the valve, but, with the esophagogastric junction in the mediastinum, reflux readily occurs. Barrett [10] feels that the integrity of the muscularis mucosae, which moves the mucous membrane, must be intact. The muscosae slides on the muscularis externae and forms a flap which covers the esophageal orifice and thus closes the valve. The earliest changes that occur in esophagitis are not visible in the distal esophageal mucosae to the endoscopist's eye but are quite evident to the pathologist in the region of the muscularis mucosae in a biopsy specimen. Inflammatory changes and fibrosis will destroy the mucosa flap valve mechanism by destroying the muscularis mucosae. How many

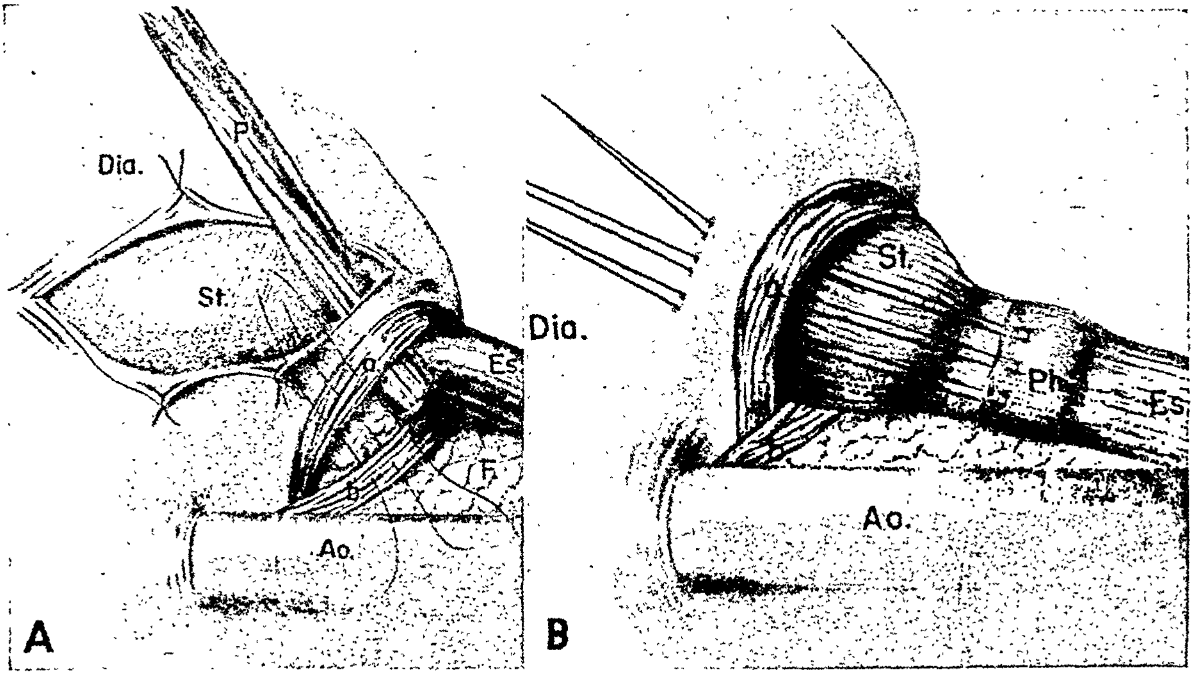

Fig. 2.—Illustration of operative area from left transthoracic approach. *A*, Penrose drain in place, with interrupted sutures placed posteriorly to approximate hiatal musculature and to narrow opening (*Ao*, aorta; *Dia*, diaphragm; *Es*, esophagus; *F*, mediastinal fat; *P*, Penrose drain, *St*, stomach; *b*, right crus of hiatus; *a*, left crus of hiatus). *B*, stomach herniated upward and phrenoesophageal ligament dissected free as membrane, with its insertion into esophagus preserved. Three sutures only (more are usually necessary) have been placed in ligament; both ends of each have been passed through hiatus and then through diaphragm from abdominal to thoracic side (*Ph*, phrenoesophageal ligament).

months or years are necessary to make these changes advance to a stage of irreversibility varies with the severity of the regurgitation and with the concentration of the irritating gastric juice.

Many "asymptomatic" persons have hiatus hernia demonstrated on barium x-ray examination with use of barium sulfate, but it is curious why they seek medical aid and have x-ray studies done. What initiates symptoms in persons with previously asymptomatic hiatus hernia is not known. We have noticed a strong correlation between the onset of symptoms with physical or emotional stress, prolonged hospitalization and recumbency, an operation not related to the stomach or esophagus, transient hyperacidity, repeated severe vomiting, and the prolonged use of an indwelling nasogastric tube.

Because of the terrifying consequences of an untreated and symptomatic hiatus hernia,[11] we strongly urge surgical repair before the irreversible changes in the submucosal layers occur. A period of adequate medical management should be tried first; however, unless the symptomatic trend is completely reversed and unless one is sure the patient will adhere to a strict medical program, surgery should be advised without procrastination.

In experienced hands either the abdominal or transthoracic approach can be used to accomplish an equally satisfactory operation. In many instances concomitant procedures can be done in the upper part of the abdomen, making this route preferable.[4] However, many surgeons today still fail to accept hiatus hernia as a cause of symptoms. During an abdominal operation a halfhearted attempt may be made at repairing the hernia, with strict attention to details not being followed, and the patient is not helped. This type of repair is mentioned only to be condemned and has nothing to offer other than antacids, bland diet, and antispasmodic drugs.

Our preference is for the transthoracic approach (fig. 2). The basic principles of an adequate repair should not be compromised; however, each surgeon has personal preferences in technical management, and these details should be varied according to necessity.

The basic principles are as follows: 1. The esophagogastric junction should be brought below the diaphragm and maintained there. 2. The peritoneal sac should be destroyed. 3. The phrenoesophageal ligament, if suitable, should be sutured to the abdominal surface of the diaphragm. 4. The fatty bare area posteriorly should be eliminated and the hiatus narrowed by approximation of the two muscular bundles of the right crus posteriorly. 5. The oblique angle of entrance of the esophagus into the stomach should be protected and maintained. If these principles are followed, the results, we feel, should be excellent.

Summary

The surgical treatment of hiatus hernia was evaluated in 65 patients. Medical management should be tried first, but, unless symptoms are relieved completely and the patient is willing to adhere strictly to a rigid medical management for many years, operation should be performed. Surgical repair resulted in 90.8% of the patients in this study becoming asymptomatic over a follow-up period of six months to seven years.

Close attention to details of the operation is mandatory for good results. The abdominal or thoracic approach can be used to accomplish the same technical results, but the basic principles should not be compromised. Our preference is for the transthoracic approach. The cardia must be reduced below the diaphragm. The hernia sac must be destroyed. The bare area posteriorly should be eliminated and the hiatus narrowed by approximation of the muscular bundles of the right crus posteriorly. The phrenoesophageal ligament should be sutured to the abdominal surface of the diaphragm, and the oblique angle of entrance of the esophagus into the stomach should be maintained.

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PRURITUS ANI ET VULVAE

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Local primary irritation is by far the most frequent cause of pruritus ani et vulvae. Other causes are contact dermatitis, specific dermatological diseases, disease of the anal, rectal, and genitourinary tracts, disease of other organs, and psychogenic disturbances. Etiological diagnosis is often difficult because pruritus from any cause can exist for only a short time before visible secondary changes are induced by scratching and medication. Anal pruritus scarcely exists in geographical areas where bathing with water and no soap or toilet paper is the custom after defecation. When an organ system other than the anogenital apparatus is involved, all local sources of irritation should be removed and conservative treatment applied until the true source of the itching sensation becomes apparent. Presumed psychogenic disturbances are made worse by treatment if the diagnosis happens to be incorrect, and the supposed emotional exhaustion rapidly disappears when the real etiology is discovered and eliminated. More time should be spent on searching out the underlying cause of anogenital pruritus. Specific sensitization to condiments should not be overlooked in unsolved cases.

For purposes of this round table discussion on anogenital pruritus, we have reviewed our last 500 cases and the voluminous literature on the subject for the past 25 years. Concepts of this symptom complex have been constantly changing. The literature is replete with articles approaching the subject from the standpoint of the surgeon,[1] the gynecologist,[2] the dermatologist,[3] the allergist,[4] and the psychiatrist.[5] It is obvious that for the proper treatment a diagnosis must be made based on etiology. Local treatment, based on the symptom of itching, may be temporarily successful, but in the long run may lead to serious disappointments and complications.

Pruritus ani et vulvae is a symptom complex of great variation. Pruritus without any visible pathology exists only for a short period of time. Very soon, changes appear in the skin and the adjacent mucous membranes. The examiner must be able to recognize the basic inflammatory process in order to make an etiological diagnosis. He must be able to distinguish between a dermatitis due solely to scratch and a dermatitis due to primary chemical irritation and a dermatitis of allergic origin. He must also be able to recognize the earliest signs of atrophy, hypertrophy, and specific inflammatory processes such as occur in lichen planus, lupus erythematosus, and parasitic infestations.

Each specialist tends to overemphasize disturbances or diseases with which he is familiar as the cause of pruritus of the anogenital region. Vulvectomies for lichen planus and perianal injections of alcohol or tattooing for perianal psoriasis have been done after inadequate examination. Likewise, prolonged dermatological therapy for anogenital pruritus without benefit is carried out when the dermatologist fails to have adequate gynecologic and proctological examination for such things as cryptitis, proctitis, and cervicitis. In our experience, some of the worst treatment failures have occurred after months of therapy[3] by a stubborn specialist who would not recognize the importance of other fields. We refer particularly to cases of pruritus vulvae due to an almost insignificant discharge from a focus of infection in the genital tract requiring the attention of a gynecologist and intractable pruritus ani treated for months by a dermatologist and found by the proctologist to be due to cryptitis in hidden pockets of infection. The following list is our classification of pruritus ani et vulvae based on etiology: (1) local primary irritation, (2) contact dermatitis (dermatitis venenata), (3) specific dermatological diseases, (4) anal, rectal, and genitourinary tract disease, (5) disease of other organs, and (6) psychogenic disturbances.

Local Irritation

The various sources of local irritation comprise by far the largest group. At first there is itching of various degrees followed by the development of a scratch dermatitis, with erythema, scaling, thickening, fissuring, hyperpigmentation, and, as a final stage, leukoplakia and possibly malignancy. The three commonest sources of irritation are (1) leukorrhea, even though minimal; (2) the daily use of toilet soap; and (3) the retention of fecal remnants in folds of the anal canal. A fractional drop of leukorrheal discharge from any cause, such as trichomonas vaginalis infection, can set up an intolerable itching which may be protracted over months and even years. In uncleanly people, who bathe infrequently, the retention of sweat and sebaceous material protects the skin and mucous

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membranes from the irritating effects of this discharge. Protective ointments and pastes have proved effective in relieving the pruritus because of their protective effect.

It is an ironic and extremely important fact that anal pruritus scarcely exists in geographical areas where bathing with water and no soap or toilet tissue is the custom after defecation. Marchionini,[6] in 1952, stated that, because of the religious precepts of Islam, after defecation only plain water was used for cleanliness and all mechanical irritation of the skin and mucous membranes was avoided, thus eliminating a medium favorable to the growth of microbes. Fecal remnants were removed and, although hemorrhoids were common, irritation did not develop. In his own practice now, in Munich, he uses dilute potassium permanganate solution for cleansing purposes after defecation. This is a practice which we have used for more than 30 years for the entire anogenital area with gratifying results.

Highly alkaline soap precipitates retained in folds and crypts produce a chemical irritation which may last for one to two weeks and, because of daily repetition, may become progressively worse. Often retention of a combination of minute fecal material and soap precipitates the pruritus. It is our firm belief that primary irritation from the abovementioned sources of irritation is the basis of at least 75% of all anogenital pruritus, although there may be secondary factors of great importance such as emotional stress.

Contact Dermatitis (Dermatitis Venenata)

Next to primary irritation, contact dermatitis is the most common cause of itching of the anogenital region. A large list of substances has been incriminated. The principal allergenic substances include local medications, toilet paper, suppositories, enema and douche nozzles, resin finishes on fabrics, drugs taken by mouth, nail lacquer, deodorants, plant oleoresins, contraceptives, and some foods. There are numerous reports in the literature of anogenital pruritus due to specific sensitization to common foods such as milk, wheat, eggs, chocolate, alcohol, fish, coffee, cocoa, beef, figs, tomatoes, asparagus, dewberries, beans, avocados, pork, prunes, peas, beets, yeast, chicken, rice, oranges, and peanuts. Some of these were confirmed with patch tests, some with intradermal tests, and others by the use of elimination diets. It has been our experience over many years that a positive patch or intradermal test is only another finding and that in all cases this must be proved clinically by withdrawal of the suspected food followed by a recrudescence after the food has been again ingested.

There is a vast difference between urticarial reaction to the protein fraction of foods and the development of a contact dermatitis due to specific epidermal hypersensitivity to an oleoresin. Urticaria due to the protein fraction of foods can always be elicited over other parts of the cutaneous surface and is never limited solely to the anogenital region. We believe that contact dermatitis due to oleoresins in certain foods and particularly condiments offers a fertile field for further investigation. We have yet to prove a localized anogenital pruritus due to specific sensitization to the oleoresins of common foods. However, we would at this time like to report a series of 11 cases of anogenital pruritus due to specific hypersensitivity to the oleoresins of condiments. Although spices have been mentioned as possible causes of pruritus ani et vulvae,[7] there are no published reports of confirmatory patch tests to any of the condiments. Mustard, pepper, cloves, cinnamon, anise, and nutmeg have been shown to be the cause of dermatitis of areas other than the anogenital region and, in some of these instances,[8] positive patch tests have been secured. In our series, in each case a battery of standardized patch tests was performed. This list included mustard, pepper, cloves, cinnamon, nutmeg, vanilla, and allspice. In each instance, where a positive patch test was secured, a flare-up of anogenital pruritus was produced on further ingestion of the suspected condiment.

The main clinical features of an anogenital pruritus due to specific sensitization to oleoresins are easily recognized. The itching begins perianally and shortly thereafter itching of the vulva and surrounding parts develops. There is a spreading contact type of dermatitis which first involves the intergluteal and perianal areas. Depending on the severity of the dermatitis, the entire area becomes confluent and the dermatitis may spread out to involve the thighs and the crural folds. In some cases, there is fluctuation in the severity, depending on the frequency of ingestion of the offending condiment. In our one black pepper case, the dermatitis was severe and continuous. In one of our cinnamon cases, the itching was pronounced for three or four days the first part of the week and subsided by the end of the week or until cinnamon was again ingested at Sunday morning's breakfast. There was wide variation in fluctuations in our mustard cases. Some were continuous, others with periods of freedom depending on the frequency of ingestion. It is well to remember that mustard is present in most salad dressings as well as meat sauces, ketchup, and chili sauce.

Contact dermatitis of the vulva without involvement of the anal area is not common. Substances commonly incriminated include local medications, suppositories, contraceptives, sanitary pads, tampons, douche nozzles, pessaries, nail lacquer, plant oleoresins, and certain medicaments excreted through the urine. All of these possibilities must be investigated when there is a dermatitis present. A unilateral contact dermatitis is sometimes due to specific hypersensitivity to nail lacquer and usually is on the left side due to contact with the fingernails of the right hand. A unilateral itching may be due to neurogenic causes, although careful investigation of all sources of irritation, including masturbation, must be made. There may be a patchy dermatitis of the eyelids, cheeks, or neck, which are the common sites of nail lacquer dermatitis.

Other Dermatological Diseases

Space does not permit a full discussion of dermatological disorders which may involve the anogenital region and which require special dermatological training for diagnosis. These diseases include dermatitis medicamentosa (especially phenolphthalein), psoriasis, seborrheic dermatitis, neurodermatitis, mycotic infection, intertrigo (bacterial), miliaria, lichen sclerosis et atrophicus, kraurosis vulvae, parasitic infestation, lupus erythematosus, lichen planus, and leukemia cutis. It is obvious that the symptoms of anogenital itching requires a thorough dermatological examination and in many cases a biopsy and complete laboratory tests.

Anorectal Diseases

Anal itching has been attributed to many anorectal disorders. In our experience, the following signs are the most common causes of this symptom: cryptitis, hemorrhoiditis, fissures, sinuses, fistulas, proctitis, neoplasm, and polyps. If uncomplicated by injudicious treatment, the itching usually remains localized to the perianal area, but occasionally itching of the genital and scrotal areas develops. A scratch dermatitis appears which with the passage of time becomes a chronic dermatitis with thickening, fissuring, and hyperpigmentation. In addition to a careful proctological examination, one must never forget that primary irritation from retained fecal material and soap in many folds and crypts may be the sole cause of inflammation of the anal ring.

Disease of Organs Other Than the Anogenital Region

Many general diseases have been incriminated as the cause of itching of the anogenital area. The commonest one in our experience is urticaria. In some patients who have occasional bouts of urticaria, their skins are in a constant subthreshold stage of urticaria. These patients develop itching of the anogenital area with extreme ease, and careful examination will elicit the basic nature of the condition with evidences elsewhere of urticaria. Endocrine diseases, including thyroid, pituitary, ovarian, and pancreatic (diabetes) have been incriminated. Neurological disturbances such as autonomic imbalance and epilepsy have been accompanied by anogenital pruritus. Other diseases mentioned in the literature include hepatic disease, renal disease, prostatitis, cystitis, appendicitis, intestinal parasites, bladder stone, vesiculitis, disease of the uterus and adnexa, lymphoma, and allergic rhinitis. We believe that in all cases where an organ system other than the anogenital apparatus is involved all local sources of irritation should be removed and conservative treatment applied until the true source of the itching sensation becomes apparent.

Psychogenic Disturbances

Three American textbooks of dermatology[9] attribute the majority of cases of pruritus ani et vulvae to some psychogenic disturbance. Their terminology varies. Many highly qualified dermatologists stress the importance of emotional factors in anogenital itching. We agree that emotional factors sometimes play major roles in anogenital itching. We believe that all emotional stress accentuates, prolongs, and magnifies the symptom of itching. However, we are firmly convinced that a careful history and thorough examination will show that psychogenic factors are secondary in the vast majority of cases. What would be a mild, insignificant pruritus ani or pruritus vulvae in an emotionally stable individual could be magnified to a major disaster in another individual under intense emotional stress. Not enough attention has been paid to the primary trigger mechanism. More careful attention to the primary cause of the itching will eliminate a large percentage of the so-called psychogenic anogenital pruritus cases. The theory that pruritus ani et vulvae is a type of hysteria in which the gratification of pruritus is analogous to gratification of libido and the pain of scratching is related to self-punishment and guilt[10] does not succeed in curing a middle-aged woman of pruritus of the anogenital region when the cause of her pruritus is a low-grade leukorrhea and washing of the parts three or four times daily with soap.

Another popular approach regards pruritus ani as a hypochondriacal syndrome based on the failure to successfully repress infantile fantasies concerning procreation and anal birth.[5] This has the appearance of picking a needle out of a haystack. In one of our pepper cases, that of the wife of a physician, and in one of the mustard cases, that of a middle-aged spinster, as well as in many of the routine cases due to leukorrhea and irritation from soap, the patients had already had a diagnosis of psychogenic or emotional basis for the cause of their itching. It has been our observation that many of these patients subjected to long, drawn out treatment for presumed psychogenic disturbances are made infinitely worse. It is startling how rapidly the emotional exhaustion disappears when the real etiology is discovered and eliminated. We would urge that much more time be spent on searching out the underlying cause of anogenital pruritus and its elimination.

Summary

The treatment of anogenital pruritus depends on the determination of the cause of the pruritus. More attention must be given to a search for primary irritants, such as the use of soap, leukorrhea, retained fecal matter, and local medications. Contact dermatitis due to specific hypersensitivity is a distinctive entity and its cause must be determined. Oleoresins in condiments should not be overlooked. Specific dermatological diseases of the anogenital area must be correctly diagnosed and treatment

based thereon. The gynecologist and proctologist need consultation with the dermatologist and certainly the reverse holds true. Anogenital pruritus in some cases may be but a symptom of an internal medical condition. Psychogenic disturbances and emotional stress are always a factor in anogenital pruritus, but they should never be assigned the primary etiological role without complete examination and consideration of all other possible causes.

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ADVERSE REACTIONS TO SULFAMETHOXYPYRIDAZINE (KYNEX)

ITS USE IN THE TREATMENT OF DERMATITIS HERPETIFORMIS

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In most cases the control of dermatitis herpetiformis may be readily achieved with sulfamethoxypyridazine. It is impossible to predict the level of maintenance dose necessary to suppress the clinical reaction, and it is similarly impossible to predict the blood levels achieved with any single unit dosage. Adverse reactions deter from the over-all usefulness of the drug. The adverse reactions observed concerned principally the skin and hematopoietic system. In addition, the gastrointestinal and central nervous system showed evidence of toxicity. The dermatological manifestations followed almost all known previously reported reactions to sulfonamide drugs. The administration of this drug requires routine assay of the blood for sulfamethoxypryidazine levels. It is the duty of the clinician to balance the benefits to be derived from any drug against the risks of its administration.

The administration of any drug to a patient is fraught with the possibility that undesirable and adverse reactions may ensue. The clinical usefulness of any drug, once the therapeutic indication has been determined, depends to a very considerable extent on whether it is likely to produce more than a minimal number of reactions when a large number of patients take the drug. If a drug fulfills a sufficiently critical therapeutic role it may continue to be prescribed despite a rather large number of undesirable reactions. It is the duty of the clinician to balance the benefit to be derived from the drug against the risks of its administration.

The administration of sulfamethoxypyridazine (Kynex) to a group of patients with dermatitis herpetiformis whose disease was otherwise incompletely controlled by other modalities of treatment resulted in a gratifying response in a sufficiently large proportion of the patients treated to suggest its further use in this disease. The advantages of

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sulfamethoxypyridazine administration were the beneficial results achieved in a majority of the patients treated and the simplification of the therapeutic program, inasmuch as treatment for the most part was given only once a day.

Data

The treatment of 20 patients with dermatitis herpetiformis represents a part of our experience with sulfamethoxypyridazine. The only criterion used in the selection of patients for inclusion in this group was that they presented the clinical morphologic picture of dermatitis herpetiformis. In some instances this clinical impression was fortified by results of skin biopsy that were compatible with the diagnosis of dermatitis herpetiformis, by patch-test reactions to anion members of Hofmeister's series, and by eosinophilia of the peripheral blood. The data on these 20 patients are summarized in table 1.

Table 1.—*Summary of Data on Twenty Patients with Dermatitis Herpetiformis Treated with Sulfamethoxypyridazine*

Case, No	Sex	Age, Yr.	Duration of Disease, Yr.	Control	
				Results	Dosage, Gm.
1	M	65	15	Incomplete	...
2	F	57	6	Incomplete	...
3	M	62	1½	Good	2.5/day
4	F	66	20	Good	0.5/day
5	M	46	14	Incomplete	
6	F	37	6	Good	1/day
7	F	63	25	Good	0.125/day
8	M	44	5	Good	1/day
9	M	19	1¾	Good	Adverse reaction
10	F	60	2	Incomplete	...
11	F	37	1	Good	0.5 in a. m.; 0.25 in p. m.
12	M	60	8	Trial unsatisfactory	...
13	M	25	8	Good	0.25 twice a day
14	M	44	1½	Good	Adverse reaction; died
15	M	45	20	Good	0.5/day
16	M	28	9	Good	0.5 every 2 or 3 days
17	M	56	¼	Good	1 every other day; 0.5 on alternate days
18	M	47	9	Good	Adverse reaction
19	F	3	7/12	Failure	...
20	M	59	3	Good	Adverse reaction

Thirteen of the 20 patients were males, the majority being in the fifth, sixth, and seventh decades of life; the ages ranged from 3 to 66 years. Only two patients had dermatitis herpetiformis for less than a year, with 13 of the 20 patients having had their disease for three years or longer. Thus, most of the patients had been subjected to a variety of treatments prior to the initiation of therapy with sulfamethoxypyridazine. The periods of follow-up varied from 2 to 11 months.

Early in the course of the study, because of a lack of appreciation of the fact that the drug would accumulate in the blood, therapy was administered in a manner similar to that employed with other sulfonamide drugs. Later it was our practice to administer 1 Gm. of sulfamethoxypyridazine during the first 24 hours of treatment, followed thereafter by 0.5 Gm. per day. Adjustment in the dosage schedule was made subsequently in accordance with the patient's clinical response.

Blood levels of sulfamethoxypyridazine were determined consistently on the patients seen during the latter part of the study, as it was recognized by tests on individual patients seen earlier that variable blood levels occurred with standard dosage schedules. For illustration, the patient in case 3 was dismissed from our care with his dermatitis herpetiformis controlled; he was instructed to continue taking 1 Gm. of sulfamethoxypyridazine a day. He subsequently recognized that this afforded an inadequate suppressive effect and on his own initiative increased his daily intake to 1.5 Gm. Still later, he took 2 Gm. routinely and, occasionally, even 2.5 Gm. per day for the desired relief. After approximately three months on this increased dosage, the concentration of sulfamethoxypyridazine was 8.7 mg. per 100 cc. of blood. On the other hand, in the patient in case 8, who took 1 Gm. of sulfamethoxypyridazine per day for three months, a concentration of 11.4 mg. per 100 cc. of blood developed.

The results of treatment of these 20 patients might be summarized as follows: good continued response, 10 patients; good response but subsequent reaction, 4; incomplete control, 4; failure, 1; and unsatisfactory trial, 1.

Control of the symptoms of pruritus and burning and eradication of the cutaneous eruption occurred in 10 of the 20 patients. By "incomplete" control we would indicate that sulfamethoxypyridazine alone was inadequate to control the eruption but when it was combined with other modalities of therapy the signs and symptoms of the disease were abated. The dosage varied from as little as 0.5 Gm. every two to three days to 2.5 Gm. per day. The usual dosage, however, was 0.5 Gm. per day taken as a single dose. The details of treatment in case 17 are presented to illustrate a good response to the treatment and to demonstrate the laboratory evaluation carried out.

Case 17.—A blistering eruption had developed in a 56-year-old man three months previous to admission. The eruption took the configuration of grouped bullae over the extensor surfaces of the arms, the anterior and posterior parts of the thorax, the buttocks, and the inguinal areas, and about the extensor surfaces of the knees. Rather intense pruritus and burning of the skin were associated symptoms. Prior to his being seen by us, steroid therapy had been administered without benefit.

The diagnosis of dermatitis herpetiformis was established on the basis of the clinical morphology of the eruption and a skin biopsy which showed a pressure or tension bulla without evidence of acantholysis.

Therapy was initiated with sulfamethoxypyridazine in a dosage of 0.5 Gm. given twice the first day and 0.5 Gm. given daily thereafter. Table 2 indicates the dosage of the drug and the blood levels achieved. On this dosage schedule there was good control of the dermatitis herpetiformis (fig. 1). During the period of observation blisters recurred a few times but these periods have been short-lived. On each of these occasions the patient could relate the relapses to long periods of hard physical labor.

Sulfamethoxypyridazine was given a clinical trial in nine patients with other dermatological diseases as follows: bullous pemphigoid, four patients; erythema multiforme, three; eczema nummulare, one, and lichen planus, one. A hemolytic process secondary to sulfamethoxypyridazine therapy developed in one of these patients, and her case will be presented in detail later in this paper. The lack of response to therapy in this group led us to believe that sulfamethoxypyridazine possesses no specific propensities for ameliorating dermatological diseases but that its therapeutic effectiveness is the antibiotic property ascribed to the sulfonamide group as a whole.

TABLE 2.—*Dosage and Blood Concentration of Sulfamethoxypyridazine in Patient in Case 17*

Date	Dosage, Oral, Gm.	Sulfamethoxypyridazine Level, Mg./100 Cc.
1/22	0.5 twice a day for 1 day; 0.5 a day thereafter	...
1/28	0.5 a day	2.4
2/5	1 twice a week; 0.5 on other days	4.5
3/25	1 every other day; 0.5 on alternate days	3.9
4/22	1 every other day; 0.5 on alternate days	5.3

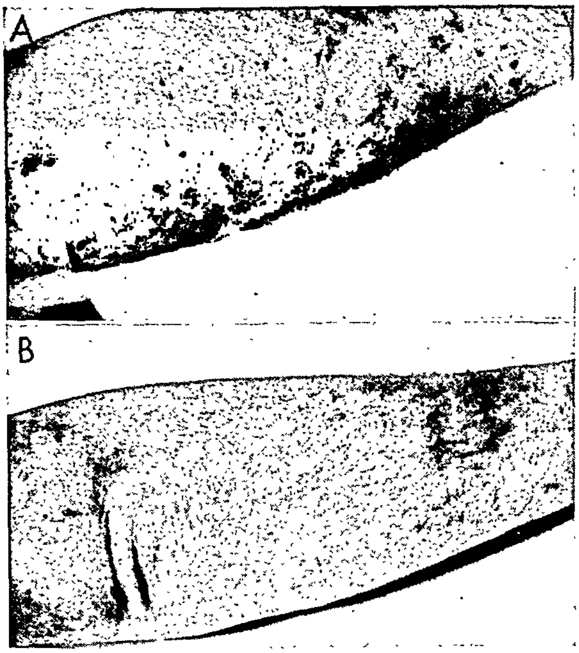

Fig. 1 (case 17).—Dermatitis herpetiformis: *A*, before treatment and, *B*, after 12 days of treatment with sulfamethoxypyridazine. This patient subsequently had leukopenia secondary to drug therapy.

Adverse Reactions

Adverse reactions to sulfamethoxypyridazine were encountered in some of the patients. Such reactions will, of course, detract from the over-all usefulness of the drug. Close observation of the patient during administration should, however, give early recognition to potentially serious reactions and prevent fatalities from occurring.

During the Second Conference on Sulfonamides, Lehr[1] reviewed the clinical toxicity of sulfonamides and listed the reactions as follows: (1) potentially serious reactions, including complications of the urinary tract, sensitization reactions (drug fever, rash, and contact reactions), blood dyscrasias, and hepatitis, and (2) milder reactions, including acidosis, cyanosis, and reactions related to the central and peripheral nervous systems.

It is interesting to note that, among the potentially serious reactions listed, only complications of the urinary tract have been unreported to date. Drug fever and cutaneous eruptions have been commonly reported, with headache and other complaints related to the central nervous system being not uncommon.

TABLE 3.—*Incidence of Adverse Reactions to Sulfamethoxypyridazine as Reported in Literature*

Author	No. of Cases	Reactions		
		No.	%	Types
Jones, W. F., and Finland, M.: Ann. New York Acad. Sc. 69:473, 1957	6	0	...	...
Lepper, M. H., and others: Ann. New York Acad. Sc. 69:485, 1957	49	0	...	...
Jackson, G. G., and Grieble, H. G.: Ann. New York Acad. Sc. 69:493, 1957	56	5	8.9	Headache, fever, eruption, abdominal pain, dizziness
Ross, S., and others: Ann. New York Acad. Sc. 69:501, 1957	14	0	...	...
Walker, W. F., and Hamburger, M.: Ann. New York Acad. Sc. 69:509, 1957	52	1	1.9	Eruption
Songco, R. S., and others: J. Philippine M. A. 33:520, 1957	36	3	8.3	Vomiting, cutaneous eruption
Velasco-Joven, E. K., and Domingo, P.: J. Philippine M. A. 33:584, 1957	3	0	...	...
Grieble, H. G., and Jackson, G. G.: New England J. Med. 258:1, 1958	63	4	6.4	Headache and maculopapular eruption common; also fever, abdominal pain, dizziness
Lindsay, D. G., and others: A.M.A. Arch. Dermat. 78: 299, 1958	85	13	15.3	Severe bullous eruption; other eruptions

Table 3 summarizes the clinical experience of other investigators with sulfamethoxypyridazine and the incidence of complications with this therapy. Tisdale[2] recently reported the additional complication of focal hepatitis in a patient receiving sulfamethoxypyridazine.

We observed a total of 28 patients—19 with dermatitis herpetiformis (one of the 20 patients had an unsatisfactory trial) and 9 with assorted dermatological conditions—and in this series five adverse reactions occurred. Case 14 was included in a preliminary report.[3] Sulfamethoxypyridazine afforded good control of this patient's dermatitis herpetiformis; however, pyrexia, arthralgia, and albuminuria developed, and these were interpreted as manifestations of a toxic reaction rather than a true reaction of hypersensitivity. When this patient was dismissed from the clinic, his general health was considered good and laboratory evaluation reflected no abnormal finding. He died about 10 days later but, because autopsy was not performed, we can only speculate on the course of events.

The patient in case 9 had an initial good response to treatment with sulfamethoxypyridazine, but on his return home a generalized erythematous maculopapular eruption developed. The patients in cases 18 and 20 each demonstrated an initial good control of the disease, only to manifest subsequently an adverse reaction characterized by leukopenia. The details of case 18 follow.

Case 18.—A 47-year-old man gave a history of a pruritic eruption, consisting of grouped vesicles and urticarial papules over the scalp, thorax, scapular areas, abdomen, and extensor surfaces of the elbows and knees, that had been present for about nine years. A diagnosis of dermatitis herpetiformis was made on the basis of the morphology of the skin lesions and a skin biopsy which showed pressure or tension bullae without evidence of acantholysis. In addition, patch tests with potassium iodide gave a positive reaction, and the eosinophil count on the peripheral blood was 3.5%. A variety of medicaments given systemically in the past had not achieved control of the condition. More recently, steroids had been tried without success.

Table 4.—*Dosage, Blood Concentration of Drug, and Leukocyte Count in Patient in Case 18*

Date	Dosage, Oral, Gm per Day	Sulfamethoxypyridazine, Mg. per 100 Cc.	Leukocytes per Cu. Mm.
1/16..........	0.5 twice; 0.5 thereafter	...	5,400
1/22..........	0.75	3.9	4,000
1/28..........	0.75	2.1	4,000
2/13..........	0.75	2.1	3,100
2/20..........	0.75	2.3	3,700
3/13..........	1	2.6	4,100
4/12..........	Discontinued	3.3	2,800
4/24..........	...	0.15	4,200

When the patient was first seen, sulfamethoxypyridazine was administered in a dosage of one tablet (0.5 Gm.) twice a day for one day and then one tablet per day thereafter. Lack of complete control later necessitated increasing the dosage of the drug. Table 4 indicates the oral intake of the drug, the concentration of the drug in the blood, and the leukocyte counts.

While the patient was receiving sulfamethoxypyridazine, his dermatitis herpetiformis remained under good control. However, after a month of treatment with a dosage of 1 Gm. per day and the attainment of a leukocyte count of 2,800 per cubic millimeter of blood, it was considered that he had a toxic suppression of the leukocytes and treatment was discontinued. A subsequent course of sulfamethoxypyridazine therapy has not been attempted.

In the group of patients with miscellaneous diseases who were treated with sulfamethoxypyridazine, there was one in whom a hemolytic process developed, most probably on the basis of use of this drug. A summary of this case follows:

Case 21.—A 64-year-old woman was admitted directly to the hospital for treatment of a generalized cutaneous blistering eruption that had been present for four months. Mucosal lesions had never been evident.

On admission, she presented a widespread bullous eruption without particular grouping; some of the bullae were seen to be arising from normal skin, while others were on an urticarial base. She had marked pruritus. Pertinent laboratory evaluation included a skin biopsy which showed a tension or pressure bulla without acantholysis. A definite diagnosis was not established. Thus, a variety of treatments, including use of sulfapyridine, diphenhydramine (Benadryl) hydrochloride, sulfamethoxypyridazine, and steroids, was instituted.

Because of lack of response to any one of these medications, a second course of sulfamethoxypyridazine therapy was given about three weeks after she had received the first course; this course consisted of 2 Gm. of the drug given daily in a single dose for eight days. Only partial control of the blistering was achieved.

On this dosage schedule the blood level of sulfamethoxypyridazine was 19 mg. per 100 cc. on Dec. 5, 1957, and, thus, administration of the drug was discontinued. When the level reached 3.5 mg. six days later, the drug was again administered in a dosage of 0.5 Gm. per day, and this dosage was continued for six additional days.

When the patient was admitted on Oct. 28, the hemoglobin level was 12.6 Gm. per 100 cc. of blood; on Dec. 3 and Dec. 7 it was 9.7 Gm.; and on Dec. 16, the day treatment with sulfamethoxypyridazine was permanently discontinued, it was 8 Gm. There was no corresponding decrease in the leukocyte count. The reticulocyte count on Dec. 16 was 7.2%. After two transfusions of 500 cc. of whole blood and inauguration of the daily administration of iron by mouth, there was a return of the blood value to normal within the next month.

The physicians of our clinic group referred patients with adverse cutaneous reactions from sulfamethoxypyridazine to us for dermatological consultation. A summary of one such case is given here because the case illustrates perhaps the commonest cutaneous reaction as recorded by those reporting adverse reactions to this drug.

Case 22.—A 26-year-old man was treated for an "influenza syndrome" with sulfamethoxypyridazine given in a dosage of 0.5 Gm. twice a day. Twenty-four hours after initiation of therapy the patient experienced increased lassitude, fever, and chills, and the following day he had headaches. He interpreted these symptoms as a part of the influenza and continued taking the drug for a total of three and one-half days (seven doses of 0.5 Gm. each).

Twenty-four hours after he discontinued taking sulfamethoxypyridazine only general malaise persisted, but then a generalized, fine, erythematous maculopapular eruption developed which was accentuated on the trunk (fig. 2). No oral lesions were present. At this time (two and one-half days after use of the drug had been stopped) the blood level of sulfamethoxypyridazine was 5.4 mg. per 100 cc.

The patient gave no history of hay fever, asthma, or migraine headaches. A sulfonamide drug had been taken on one occasion previously without reaction, but in the past he had reacted to penicillin with urticaria. With antihistamines taken by mouth and soothing topical treatments, the skin reaction abated in 72 hours.

The entire group of sulfonamide drugs is known to produce fixed drug reactions, and sulfamethoxypyridazine is no exception in this regard. To our knowledge, a fixed drug reaction has not previously been reported, although there is no reason to presume it would not eventually occur.

Case 23.—A 29-year-old woman had been receiving care for recurrent infections of the urinary tract. Prophylactic treatment with sulfamethoxypyridazine had been advised in a dosage of 0.5 Gm. given daily on five successive days during every two-to-three-week period. Her dermatological complaint was of an intermittent presence of a pruritic erythematous plaque on the dorsum of the right third finger; this condition would persist for five to seven days and then disappear (fig. 3). It was only after direct questioning that she associated the skin eruption with the ingestion of sulfamethoxypyridazine. We interpreted her skin eruption as due to a fixed drug reaction. She had taken sulfonamide drugs previously without untoward reaction. She gave no history of hay fever, asthma, migraine headaches, or urticaria.

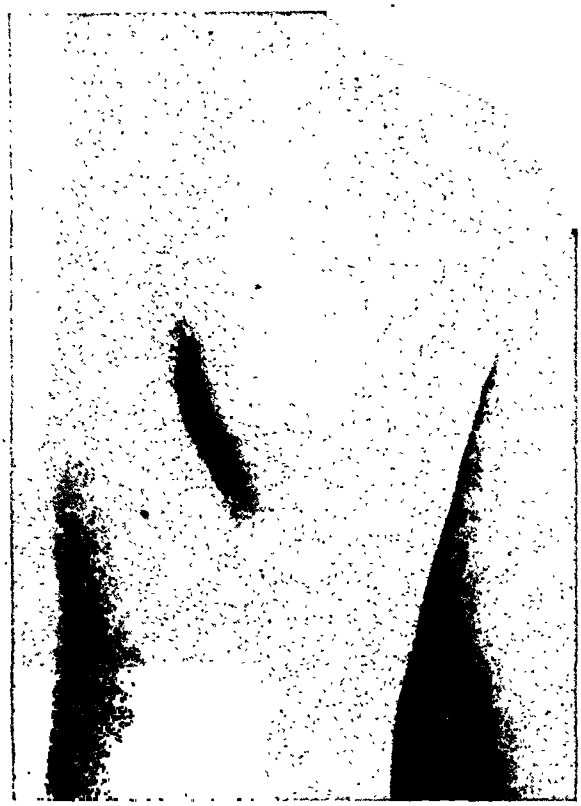

Fig. 2 (case 22).—Erythematous maculopapular eruption seen secondary to treatment with sulfamethoxypyridazine for influenza.

Reactions of photosentivity can be anticipated in patients taking the sulfonamide drugs. A summary of such a case follows:

Case 24.—A 61-year-old farmer had had intermittent sore throat for four months. Among the drugs prescribed were tetracyclines, to one of which a cutaneous reaction developed. About five weeks prior to consultation with us, the patient took sulfamethoxypyridazine in a dosage of two tablets (1 Gm.) the first 24 hours and one tablet a day for the next four days. After this course of treatment an eruption developed on the sun-exposed portion of the body; this occurred during the period he was spending much time in the sun preparing his farm land for spring planting. Examination disclosed an eczematoid reaction of the face and ears (with sparing of the forehead) and of the dorsum of the hands and forearms. This patient gave no history of atopy but had previously had adverse reactions to a tetracycline preparation and to succinylsulfathiazole (Sulfasuxidine).

The employment of sulfamethoxypyridazine by us and other physicians, and our seeing the subsequent development of adverse reactions in some of these patients, alerted us to the fact that the drug was not without the potentialities of producing still other reactions which might in themselves be a more serious threat to the life of the patient than the original disease under treatment.

Comment

The unique pharmacological properties of sulfamethoxypyridazine are its low degree of acetylation and its slow renal clearance. The acetylated form is cleared faster from the blood than is the non-acetylated form. This medicament shares with sulfapyridine, sulfoxone (Diasone) sodium, and Promacetin (sodium 4, 4′-diaminodiphenylsulfone-2-*N*-acetylsulfonamide) a low degree of acetylation. The fact that drugs which suppress dermatitis herpetiformis have a common pharmacological property is of interest. The pharmacology and physiology of sulfamethoxypyridazine have recently been reviewed.[4]

In most cases the control of dermatitis herpetiformis may be readily achieved with sulfamethoxypyridazine. This control can be maintained with low daily doses in most instances. Occasionally, a patient has taken as much as 2.5 Gm. a day to control his eruption without suffering ill-effects. The control is as good as that exercised by any of the other suppressive drugs used in the treatment of dermatitis herpetiformis.

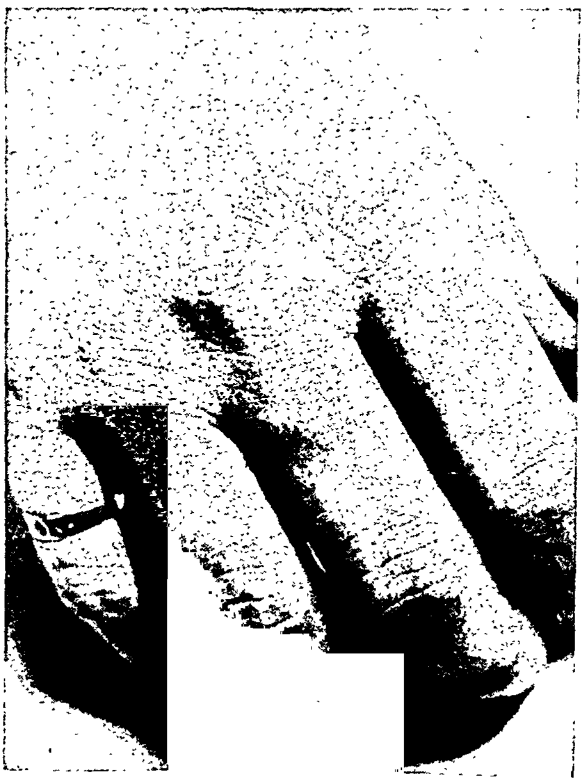

Fig. 3 (case 23).—Fixed eruption occurring over dorsum of right third finger in patient taking sulfamethoxypyridazine as prophylaxis against recurrent infections of urinary tract.

The maintenance of high blood levels for 24 hours on a single dose of the drug as a result of its low renal clearance is of tremendous help in suppressing the eruption. In these circumstances it is possible for the patient to take one dose of the drug daily and for control to be maintained. It is a great convenience to patients, and, consequently, it is easier to gain their cooperation.

Just as it is impossible to predict the level of maintenance dose necessary to suppress the clinical reaction, it is similarly impossible to predict the blood levels achieved with any single unit dosage. While blood levels of 2 to 4 mg. per 100 cc. were obtained in most patients on daily maintenance doses of 0.5 Gm. of the drug, in some instances high blood levels were obtained with exactly similar dosages and in one instance a patient who was taking 2.5 Gm. per day had a relatively low blood level. Because of the danger of cumulative concentrations with the drug, routine studies of the blood and routine urinalyses should be made and also blood levels of sulfamethoxypyridazine need to be determined at various intervals to correlate the surface control with the unit dosage and the blood level achieved with that dosage. It seems apparent that this is the only safe way to administer this medicament over a long period.

The adverse reactions observed concerned principally the skin and hematopoietic system. In addition, the gastrointestinal and central nervous systems showed evidence of toxicity, as was described. The dermatological manifestations followed almost all known previously reported reactions to sulfonamide drugs. They all responded promptly to cessation of treatment with the drug and institution of appropriate therapeutic measures. No crystalluria has been observed. One original difficulty in the use of this medicament was the development of toxic reactions due to high blood levels. This included malaise, arthralgia, fever, and eruption. This type of reaction was perhaps the most serious encountered. There is no way of knowing precisely whether it contributed to the death of the one patient who, three weeks after having such a reaction and recovering satisfactorily as far as clinical and laboratory evidence was concerned, died suddenly under unusual circumstances described by the home physician as indicative of adrenal exhaustion.

The adverse reactions limit the usefulness of sulfamethoxypyridazine in therapeutic dermatology. However, it should be noted from the other series reported in table 3 and from our experience that the drug may be administered with a certain degree of safety once the method of administration is understood and treatment is given with appropriate safeguards, namely, determinations of the blood level of the drug, studies of its hematopoietic effects, and analyses of the urine. Without such safeguards it is obviously impossible to gauge the effectiveness of the medication or the possibilities of potential reaction. Drug reactions have always been a part of the administration of sulfonamide medicaments. In many instances they have been an accepted risk because of the usefulness of the particular medication. Sulfapyridine has an extremely poor pharmacological reputation. Yet, it is used routinely in dermatology for the suppression of dermatitis herpetiformis. We recently observed one patient who took 20 grains (1.29 Gm.) of sulfapyridine three times a week for 14 years without incident. The amount of sulfapyridine that is used in dermatology, in spite of the apparent pharmacological hazards, indicates that a drug may be useful in certain areas of medicine once its limitations and dangers are fully appreciated.

Summary and Conclusions

Adverse reactions to sulfamethoxypyridazine in this study were due to the toxic effect of cumulative dosage; these involved principally the hematopoietic and cutaneous organs. To our knowledge, a fixed drug reaction and the reaction of photosensitivity to sulfamethoxypyridazine have not previously been reported.

Sulfamethoxypyridazine was found to afford good control of dermatitis herpetiformis in 10 of 20 patients. Therapeutic control of the eruption was achieved in most instances with a single daily maintenance dose. There is no predictability in the relationship between the dose administered and the blood level obtained over long periods. Therefore, the administration of this drug requires routine assay of the blood for sulfamethoxypyridazine levels.

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CLINICAL NOTES

PRESERVATION OF NATURAL LANDMARKS IN UNILATERAL CLEFT LIP

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The harelip deformity, with its twisted distortion of the nose and gaping cleft of the lip, utterly disfigures the center of the face and destroys any chance of normal expression—even a smile is grotesque. So horrible is it that whatever the surgeon does will be an improvement. Yet, mere improvement is not enough and should not be accepted as a triumph. Rather, it is felt that, until these anomalies can be prevented, the surgical approach must be designed artistically so as not only to obtain a closure of the cleft but to camouflage it.[1]

Five years ago there was a constant trickle of patients with harelip to Kum Chon Korean Hospital, which services the population from a multitude of hutted villages in an area north of Seoul. Various degrees of this deformity were represented, and, after months of exposure to and stimulation from the problem, it began to dawn on me that all components of a normal lip and nose were more or less present in each person with cleft lip, depending on the severity of the deformity.

The Operation

If this were true, the primary step in construction would be to recognize all existing landmarks and juggle them out of distortion into normal position. Closer observation revealed, on the noncleft side, two-thirds of the cupid's bow, one philtrum column, and the associated dimple. As an entity they are drawn up toward the columella in an almost unrecognizable distortion (fig. 1*X*), but they are available and should be brought into use by a rotation incision under the columella that will drop the entire component *A* into correct position (fig. 2). This action will leave a triangular gap under the base of the columella which can be filled by a triangular advancement from the cleft side.

The cleft side, being primarily deficient, should not be called on to do more than is absolutely necessary. Yet, quite effectively and without undue strain, it can produce from its upper portion an adequate triangular flap to match the rotation gap. Of course, when the cleft is incomplete the bridging portion easily forms the leading point of the triangular flap *B* (fig. 2*W*). When the cleft is wide, a relaxing incision under the alar base is carried up into the nostril floor to pick up the point of the triangular flap *B*, which is to be advanced from the lateral lip element (fig. 2*X*). The advancement of this lateral triangular flap *B* not only fills the gap under the columella but also has a narrowing effect on the flaring alar base and wide nostril floor (fig. 1*Y* and *Z*). To facilitate this lateral advancement

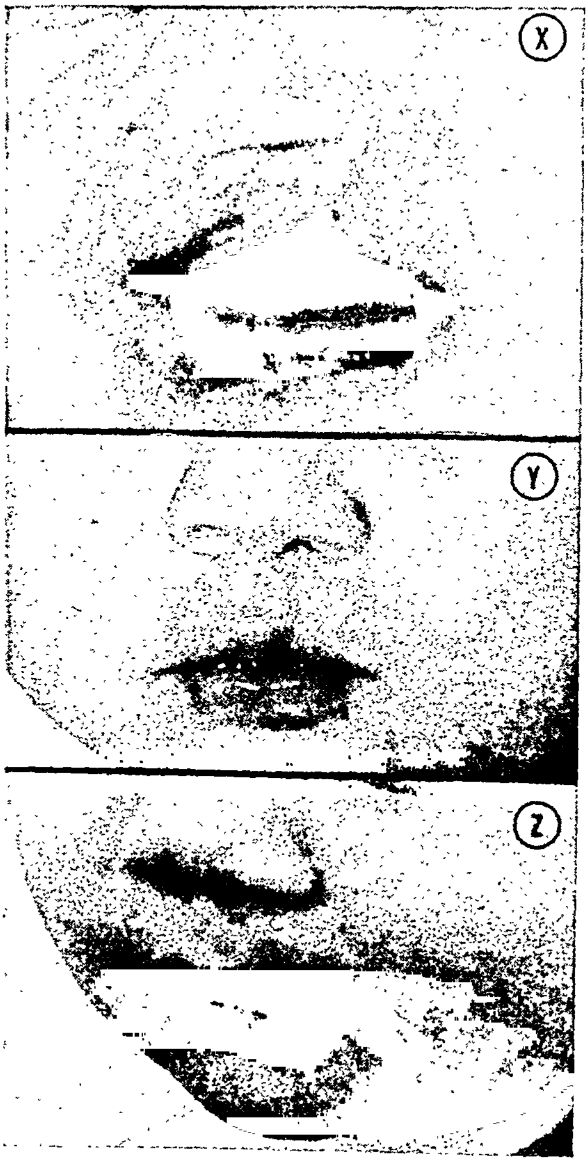

Fig. 1.—*X*, natural landmarks are distorted but present. *Y*, one month after surgery, cupid's bow and philtrum dimple have been maneuvered into normal position. Curving scar is still angry and slightly contracted. *Z*, three months later the scar has paled, smoothed out, and all but disappeared into the philtrum line.

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the lip and nose on the cleft side must be freed from their attachment to the maxilla by extensive undermining. Closure must be meticulous and pinpoint accuracy achieved in the approximation of the cleft at the white rolled edge of the cutaneous junction with vermilion. Chromic catgut sutures, 00000, are used in the muscle and mucosa membrane and silk sutures, 000000, in the skin.

Postoperative Care

A Logan bow is applied to protect the lip during the healing phase, and the suture line is sealed off from nasal discharge with bacitracin ointment three times daily.[2] Formula feedings are resumed as described by MacCollum and Richardson [3] with a 1½-in. extension of soft rubber catheter fitted to the end of a 10-cc. Asepto syringe. The catheter is eased in over the tongue, and constant pressure on the bulb produces a gentle flow of formula without the necessity of the healing lip puckering into traumatic sucking movements. The arms are restrained to keep the hands out of the mouth, and in the more acrobatic babies the legs are restrained to keep the feet out. On the fourth postoperative day the skin sutures are removed, and after one month the mother is instructed in gentle massage of the lip scar against the underlying gum with lanolin. For many weeks the scar will be hard, red, and slightly contracted (fig. 1Y), but as the months pass it will soften, relax, and pale out until it is almost invisible in its position as a philtrum line (fig. 1Z).

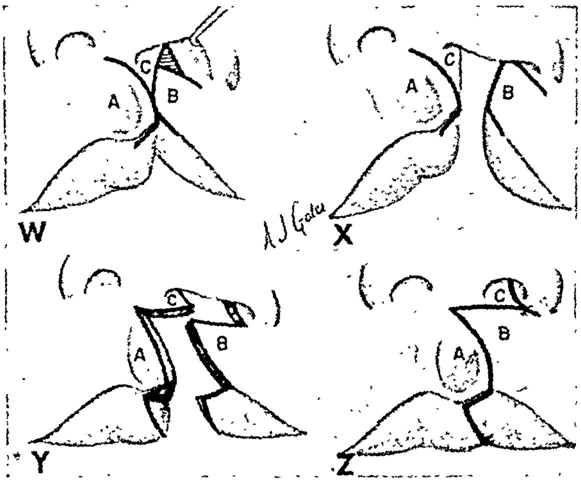

Fig. 2.—*W*, in incomplete clefts, lateral advancement flap *B* incorporates Simonart's band as its leading point. *X*, in complete clefts the lateral advancement flap *B* is developed by relaxing incision under alar base and picks up its leading point from lateral nostril floor. *Y*, flap *A* is rotated down and flap *B* advanced across cleft into rotation gap. Little flap *C* completes puzzle by interdigitating across floor of nose to straighten deviated columella, form nostril sill, and shoulder part of tension of lateral advancement. *Z*, Cupid's bow and entire philtrum dimple are now in normal position. Alar flare has been corrected. Resulting scar first curves to imitate the opposite philtrum column, then zig-zags out of sight as nostril sill and into nasal floor.

Timing the Operation

The optimum time for closure of cleft lip varies. If the deformity is minimal, operation can follow birth by a few hours. In my opinion this dash from womb to operating room is unnecessary, no matter how urgent the cosmetic emergency may seem. With an Asepto harelip feeder, feeding is no problem. Anxious parents can be pacified if it is explained that not only will the infant withstand anesthesia and operation better at 1 month of age but a more perfect lip and nose correction is likely to result.

If the cleft is severely wide, I feel it is extremely important to let the infant's tissues grow and enlarge for at least three months, after which surgical closure is relatively simple. When there is an associated cleft of the palate the principle of early closure as championed by Kilner [4] is favored. Palate clefts, in my opinion, should be corrected before the child begins to talk, anywhere from 10 to 12 months, depending again on the severity of the cleft. A gentle, well-planned operation should have minimal effect on the growth of the facial bones and still provide the child, from the outset, with an adequate mechanism with which to develop normal speech.

Summary and Conclusions

It never ceases to be a thrill that two simple incisions can set up a consecutive chain of happy actions: 1. The cupid's bow component, carrying with it one philtrum column and the entire dimple, drops into normal position, leaving a triangular gap above. 2. Advancement of the lateral lip element to fill this gap not only narrows the alar flare and wide nostril floor but unites the cleft along a curving line which simulates the one missing link, the matching philtrum column.

Several popular methods in use today ignore one or more of nature's landmarks and, what seems even more tragic, by actually destroying them in the primary repair cause them to be lost forever.

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AN IMPROVED VAGINAL APPLICATOR

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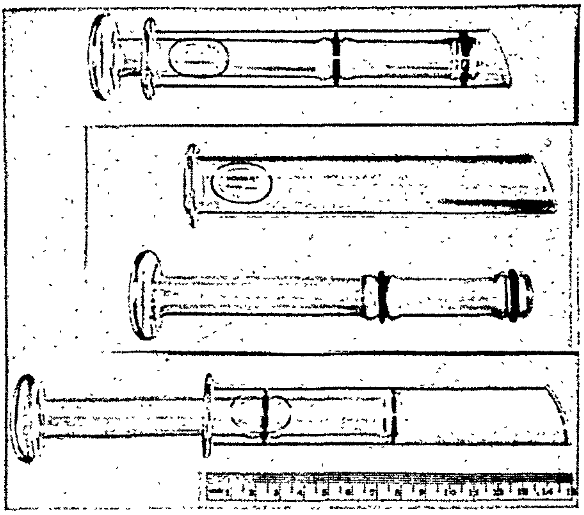
The office treatment of vaginal disorders by the local application of various powders, creams, and jellies is common practice. Most of the jellies, creams, and such are injected with syringe-type applicators usually supplied by the pharmaceutical manufacturers of the drug being used.

The placement of different powder preparations is not satisfactory, as a rule. The plastic squeeze containers, which are used to blow a stream of powder into the vagina, succeed in filling the speculum, but a minimum amount of the powder remains in the vagina itself. Another type, which blows up the vagina under pressure and forces the powder in simultaneously, seems too dangerous for use. The applicator shown (see figure) was designed to overcome certain difficulties. It will deliver a definite measured amount of any kind of preparation to the far end of the vagina without the slightest waste, under no pressure, and with no discomfort to the patient. It should be remembered, however, that some risk accompanies the use of this or any other such device in pregnant women. No instance of trouble, such as embolism, has thus far occurred in such cases with this device, but the possibility should be kept in mind.

It is a syringe made of heavy Pyrex glass, with a beveled end to facilitate insertion (see figure, *top*). The plunger, when pushed in as far as possible, automatically stops and simultaneously empties the barrel completely (see figure, *center*). The plunger has two neoprene rubber rings so arranged that the glass of the plunger does not touch the inside of the barrel. The applicator is easily sterilized and would be hard to break.

To use, the plunger is withdrawn and a little lubricant jelly is placed on each neoprene ring and the plunger replaced. The chosen amount of the selected medicament is then put in the barrel with the plunger drawn back (see figure, *bottom*), the tip of the barrel is lubricated slightly, and the tip is then inserted to the proper location, the plunger pushed all the way down, and the syringe withdrawn.



Top, applicator almost closed. When plunger is pushed in as far as possible, barrel is automatically emptied. *Center,* note construction of plunger. Glass side of plunger does not come in contact with inside of barrel and rides squarely on the two rings. *Bottom,* rings have been lubricated and barrel filled with desired amount of powder.

This applicator is very simple to use, is of rugged construction, has maximum efficiency, and can be used with any preparation. It can be supplied in any desired dimensions, though the size shown is the adult size generally used.

617 Medical Towers (25).

This applicator is manufactured by Scientific Glass Blowing Company, Houston, Texas.

LIPOPROTEINS.—Some gerontologists claim that atherosclerosis is a natural process of aging. The possibility of the occurrence of coronary artery disease at any age, even in childhood, and the failure of finding atherosclerosis in some individuals attaining the age of eighty or more years, leads one to suspect that atherosclerosis is a disease state rather than a natural process. The present popular concept is that it is an alteration of fat metabolism. The plasma lipids in man are made up principally of esters of fatty acids and glycerol; which are the neutral fats or triglycerides, phospholipids, which are fatty acids in combination with phosphorus and nitrogen compounds, cholesterol, and cholesterol combined with fatty acids or cholesterol esters and free fatty acids. These lipids are too insoluble in water to exist in solution in the body fluids and therefore with the exception of fatty acids they are combined with globulin, forming a group of large molecular substances called "lipoproteins."—J. H. Hodges, M.D., Cholesterol and Vascular Disease, *The West Virginia Medical Journal,* October, 1958.

DIAGNOSTIC PROBLEMS

ERYTHREMIA (POLYCYTHEMIA VERA), RADIATION THERAPY, AND LEUKEMIA

Clinical Pathological Conference (PM 1187-57), Oct. 24, 1957, from the Department of Pathology and the Hektoen Institute for Medical Research of Cook County Hospital, Chicago, presented for publication by Daniel S. Kushner, M.D., and Paul B. Szanto, M.D.

Clinical Data

A 37-year-old woman was admitted to Cook County Hospital on July 31, 1957, complaining of shortness of breath, loss of appetite, and a rash. Two weeks before admission, she developed an eruption consisting of large tender "knots" mainly over the knees and anterior aspect of the legs, with only a few on the arms. The lesions progressively increased in size and number for about a week, then gradually regressed. At the height of the eruption, she complained of anorexia, nausea, and night sweats and had a temperature of 100 to 101 F (37.8 to 38.3 C), with one elevation to 103.2 F (39.5 C). She had no chills or joint pains. On the day before entry, she noted increasing substernal pain, aggravated by deep breathing, and a harsh, rasping, nonproductive cough. During the present illness, she also had complained of weakness, dizziness, exertional dyspnea, orthopnea requiring two to three pillows, loss of taste for cigarettes, nocturia (two times), and "reddish" urine. She admitted to ordinarily drinking only an occasional beer.

She had been closely followed in another clinic for six years. In 1950, she inadvertently noted a mass in the left upper abdominal quadrant that was regarded by her physician as an enlarged spleen. In February, 1951, she suffered a fall, and, in the course of examination at the other clinic, splenomegaly (20 cm.) and erythremia (polycythemia vera) were observed.

Basal metabolism and I^{131} uptake were normal. Sternal marrow aspiration revealed cellular marrow, increased megakaryocytes, and erythrocyte-leukocyte ratio of 1:1, normoblastic erythropoiesis, toxic granulopoiesis, moderate increase in histiocytes, and platelet clumps. About 20 phlebotomies were performed between 1951 and 1953. In 1952, radiation therapy to the spleen was followed by some decrease in its size. Subsequently, the extremities were irradiated. For one year, she was given triethylene melamine (TEM). In June, 1954, bone marrow aspiration revealed no spicules and large numbers of megakaryocytes among the fibrous strands, and cortisone was given. TEM was again given from March to November of 1956. An intravenous pyelogram showed a hypoplastic left kidney, compensatory hyperplasia of the right kidney, and splenomegaly. During these six years of clinical observation, the patient had remained entirely free of symptoms. History revealed only tonsillectomy in 1950, and treatment for "pus tubes" in 1943. The patient's father died of diabetes and her mother of hypertension.

Physical examination revealed a thin, young woman, appearing acutely and chronically ill. Her temperature was 101 F (38.3 C), pulse rate 120 per minute and regular, and blood pressure 90/60 mm. Hg. Scattered over the anterior aspect of both legs and the ulnar aspect of the right arm were several deep cutaneous nodules (2 by 2 cm. in diameter), which were indurated and tender but not discolored. The superficial cervical veins were slightly distended. The heart and lungs were normal. The spleen extended four fingerbreadths below the costal margin. The liver edge was just palpable. No other masses were palpated. The abdomen was soft and nontender and intestinal sounds were normal. Rectal, pelvic, and neurological examinations were normal.

Urinalysis was negative. Results of hematological examinations are shown in the table. The blood Kahn test was negative. A roentgenogram of the chest taken July 13, 1957, revealed normal heart and lungs; views of the left shoulder taken Aug. 22 were normal. An electrocardiogram was unremarkable, except for sinus tachycardia. The blood nonprotein nitrogen level was 36 mg. per 100 ml., glucose level 158 mg. per 100 ml., total serum proteins 5.4 Gm. per 100 ml., albumin level 4.4 Gm. per 100 ml., globulin level 1.0 Gm. per 100 ml., gamma globulin level 0.79 Gm. per 100 ml., cholesterol level 78 mg. per 100 ml., and cholesterol esters 39%. Cephalin flocculation was negative, thymol turbidity 4.1 units, icterus index 9 units, alkaline phosphatase level 3.1 Bodansky units, and blood uric acid level 9.1 mg. per 100 ml. A urine culture taken Aug. 1 produced Klebsiella, aerogenes type, sensitive to tetracycline, chloramphenicol, streptomycin, nitrofurantoin, and sulfisoxazole. Agglutinations for typhoid, paratyphoid, and brucella were negative. A

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blood culture taken Aug. 7 revealed a hemolytic Staphylococcus pyogenes var. albus (coagulase negative). On three subsequent occasions hemolytic Staphylococcus pyogenes var. aureus (coagulase negative) was cultured. The first of these was taken while the patient was receiving tetracycline therapy and the others while she was receiving streptomycin and para-aminosalicylic acid (PAS). The organism was sensitive to penicillin, erythromycin, tetracycline, and chloramphenicol. A direct Coomb's test and lupus erythematosus preparation were negative. Aspirations of sternum and iliac crest were performed Aug. 1, but no marrow elements were obtained. On Aug. 5 a surgical biopsy of the sternum was performed and revealed small clusters of anaplastic cells (stem cells or blasts).

*Hematological Data**

Date	Hemoglobin Level, Gm.	Hemoglobin Level, %	Red Blood Cell Count, per Cu. Mm.	White Blood Cell Count, per Cu. Mm.	Hematocrit Reading, %	Neutrophils, %	Band Forms, %	Basophils, %	Lymphocytes, %	Monocytes, %	Blasts, %	Premyelocytes, %	Myelocytes, %	Metamyelocytes, %	Histiocytes, %
1951†	16.7	...	8,700,000	17,500	51	78	...	...	21	...	...	...	...	...	...
1952	11.7	...	6,600,000	21,600	...	80	7	...	11	2	...	...	...	...	...
1953	13.0	...	6,500,000	10,000	45	...	...	...	...	...	...	...	...	...	...
1954	15.6	...	5,100,000	2,000	51	...	...	...	...	...	...	...	...	...	...
1955	...	...	...	1,600	30	...	...	...	...	...	...	...	...	...	...
2/1/56	...	...	...	8,200	53	...	...	...	...	...	...	...	...	...	...
8/9/56	...	...	...	3,850	34	...	...	...	...	...	...	...	...	...	...
2/2/57	...	...	...	2,500	35	...	...	...	...	...	...	...	...	...	...
6/12/57	...	...	...	3,000	35	...	...	...	...	...	...	...	...	...	...
7/31/57	...	...	2,200,000	...	43	...	...	...	...	...	...	...	...	...	...
8/1/57	...	...	...	4,400	...	13	5	1	38	12	14	7	4	6	...
8/2/57	...	42	2,950,000	3,100	...	...	...	...	...	...	...	...	...	...	...
8/7/57	...	37	3,000,000	4,900	...	19	20	...	17	43	3	4	3	1	...
8/13/57	...	45	3,000,000	16,000	...	9	5	...	28	18	21	8	9	12	...
8/24/57	...	37	2,630,000	14,900	...	15	3	3	28	13	15	11	3	16	3
8/29/57	...	30	2,030,000	40,400	...	4	2	1	32	5	28	13	4	10	1
8/31/57	...	44	3,000,000	...	...	...	...	...	...	...	...	...	...	...	...

* Blood showed anisocytosis, poikilocytosis, hypochromia, microcytosis, polychromatophilia, stippling, few nucleated red blood cells, Dohle bodies, burr cells, tear drop cells, and toxicity.

† Platelet count was 340,000 per cubic millimeter and eosinophils 1%.

On the day after admission, the patient complained of severe substernal pain which radiated to the back, accompanied by dyspnea and restlessness. Two blood transfusions produced marked symptomatic improvement. Her temperature, initially 101 F (38.3 C), rose progressively in the first 10 days to 105 F (40.6 C), despite the successive administration of tetracycline, penicillin, and streptomycin. On the seventh day, a chill was followed by a temperature rise to 105 F (40.6 C) and a complaint of severe pain in the right foot. An area of exquisite tenderness, slight swelling, and warmth was noted on the lateral aspect of the foot, beneath, and just posterior to the malleolus. A harsh grade 3 systolic murmur was heard at the base of the heart. No petechiae were seen. Penicillin therapy (1,200,000 units a day) and streptomycin therapy (1 Gm. a day) were continued. The spleen now extended six to seven fingerbreadths below the costal margin. Urinary urobilinogen was still negative. Cortisone therapy (200 mg. a day) was begun on the 10th day, after which the right ankle pains entirely subsided. Again, symptomatic improvement was gratifying, and, for the next 10 days, her temperature remained between 99 and 100 F (37.2 and 37.8 C). A Mantoux skin test (1:1,000) was negative. Therapy with PAS was begun, and streptomycin therapy was continued.

On the 20th day, new, tender, deep, cutaneous nodules appeared. The spleen had enlarged to the iliac crest and extended 8 to 10 fingerbreadths below the costal margin. She began to complain of left shoulder pain, accompanied by tenderness and warmth, and her temperature rose to 103 F (39.4 C). The administration of eight tablets of colchicine produced dramatic relief of pain. Prednisone, 20 mg. per day, was substituted for cortisone, and the patient was placed on a Sippy regimen. Because of persistence of fever, penicillin therapy was reinstituted (1,200,000 units per day), with apparent response. Consequently, and in view of the repeated isolation of staphylococci from the blood, 20 million units of penicillin were given daily in intravenous infusion. Although three additional blood transfusions and 10 cc. of gamma globulin were given supportively, her temperature rose to levels between 101 and 104 F (38.3 and 40 C); she became increasingly dyspneic and tachypneic and complained of severe splenic pain. Her blood pressure fell to 78/50 mm. Hg, and her pulse rate was 120. The liver extended four to five fingerbreadths below the costal margin. The spleen extended into the pelvis, and epigastric tenderness was noted. The basal cardiac murmur persisted, and P_2 was noted to be loud and split. A loud to-and-fro friction rub was heard over the liver. Slight ankle edema was present. She was given oxygen and digitalis but died Aug. 31 after six weeks of acute illness.

Clinical Discussion

Dr. Steven O. Schwartz: The problem for discussion is that of a 37-year-old woman with a six-year history of illness, beginning with an asymptomatic splenomegaly and erythremia, who was vigorously treated and whose course terminated with six weeks of acute illness, characterized by an erythema nodosum, fever, sweats, arthritis, hyperuricemia, severe anemia, cardiac murmurs, staphylococcemia, pericarditis, cardiac failure, and invasion of the blood by primitive cells. The question is not why this patient died but rather why she developed an acute leukemia and what the preexisting disease was for which she was so extensively treated.

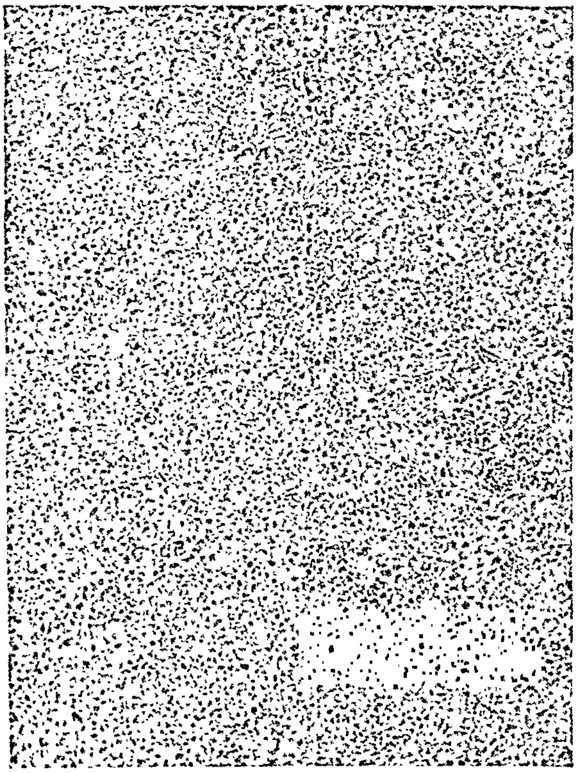

Fig. 1.—Section of liver showing accumulation of mononuclear cells in the sinusoids. Cell types at this magnification cannot be identified.

To begin with, one is reluctant to accept the diagnosis of a polycythemia vera in a 30-year-old woman, even though she had a splenomegaly and erythremia, because this is not a disease of the young, but usually of older persons. One then considers other possible bases for erythremia and splenomegaly. First, there is tuberculosis of the spleen, as the consequence of hematogenous dissemination. Against this are the negative chest roentgenogram and her failure to respond to rather vigorous antituberculous therapy. She also had a negative tuberculin skin test. Admittedly, this was done only in a 1:1,000 dilution and, therefore, some might question its validity, and one must also recognize the possibility of anergy in miliary tuberculosis. Finally, in the repeated studies, there were no radiologically demonstrable calcifications in the spleen. On the basis of these factors, it is unlikely that she had tuberculosis of the spleen.

The second possibility is that we are dealing with a myelofibrosis and a compensatory metaplasia in the spleen and erythremia, but the fact that in 1951 she had a normal marrow, with normal myelocyte production, excludes this diagnosis. Therefore, we must conclude from the evidence presented that her original disease, in 1950, was indeed a polycythemia vera, rather early and well compensated. It should again be emphasized that at that point diligent attempts should have been, and probably were, made to rule out the possibility that this was a primary tuberculosis of the spleen. The question next arises as to why this patient was so energetically treated. At no time did she have symptoms. Certainly, to give such intensive x-ray and TEM therapy at the age of 30 as to produce profound leukopenia which lasted over the period from 1954 to 1957 was hardly justifiable, regardless of one's therapeutic enthusiasm. Nonetheless, in spite of the enlarged spleen, the patient apparently got along fairly well until 1957, when she developed an acute leukemia.

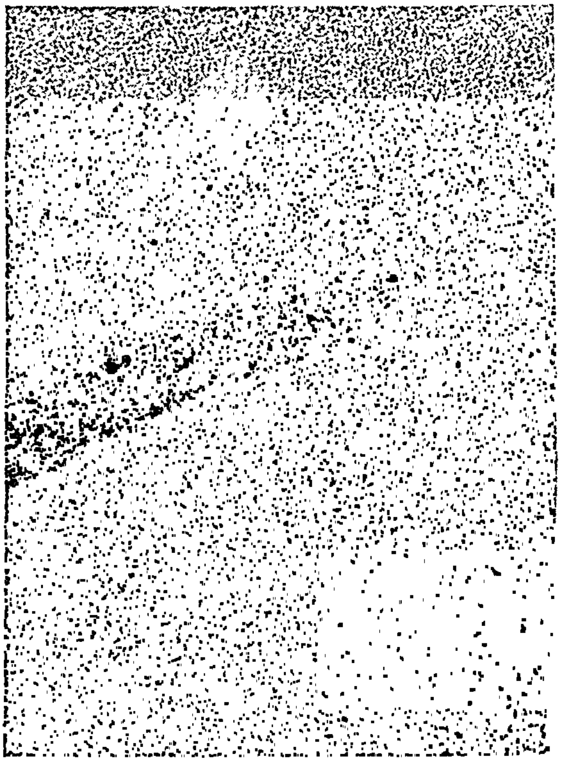

Fig. 2.—Section of spleen showing replacement of splenic parenchyma by fairly uniform type of cells. Megakaryocytes are scattered throughout.

There are a number of theoretical explanations but no factual explanations. Therefore, we must resort entirely to hypothesis. The first and the simplest is to say that this was a polycythemia vera which developed into leukemia after six or seven years. There is a popular misconception that 10% of patients with polycythemia develop leukemia. If, however, one studies the literature carefully, one finds that patients with polycythemia, who eventually develop leukemia, have at some time been treated with one form or another of radiation therapy. Even more interestingly, with orthodox x-ray therapy, it takes about five years for the development of leukemia, and usually this is a chronic rather than an acute leukemia. This record has been improved on, since it is now possible to produce acute leukemia in two years. The minority opinion, therefore, in this controversial matter, is that x-ray treatment in polycythemia vera is not only not the treatment of choice but is definitely contraindicated.

If one accepts the thesis that this patient had polycythemia vera and, in some way related to intensive and prolonged radiation therapy, subsequently developed leukemia, we must deal still with the question of why the leukemia developed. The TEM might also have played some role in its development.

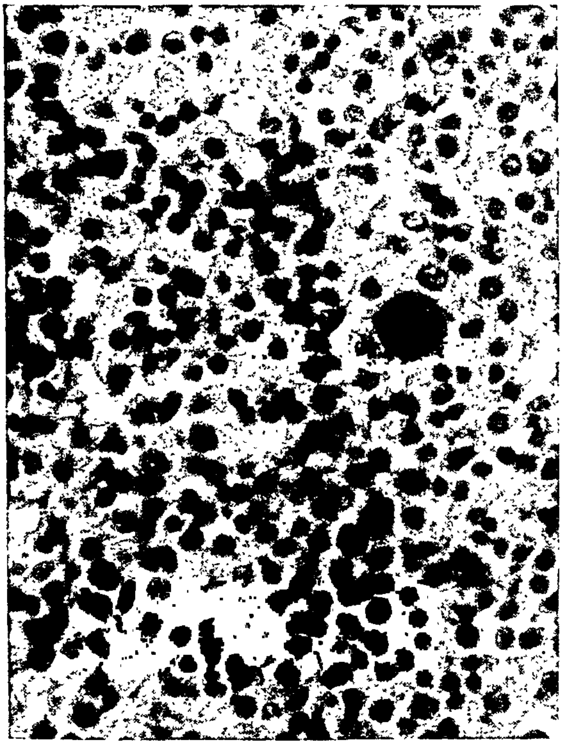

Fig. 3.—Higher magnification. Many cells belong to myeloid series—myeloblasts and myelocytes.

If one does not believe that this patient had a preexisting disease which predisposed her to develop leukemia, then one must find still another explanation. The concept of the myeloproliferative disease syndromes, currently in vogue, permits one to accept an initial proliferation of the erythrocytes, later proliferation of fibrous tissue elements, and eventually proliferation of the white blood cells. One could also look on x-rays as carcinogenic and think of the leukemia in this patient as having been produced by the x-rays. One might assume, however, that the roentgen radiation simply predisposes these patients to the development of leukemia. This seems to us the most interesting of all the hypotheses. We know that leukemia develops much more frequently in those who have been exposed extensively to roentgen rays than in the whole population. Unless one thinks of x-rays as being carcinogenic, one must assume that the x-rays simply make these people more susceptible to leukemia.

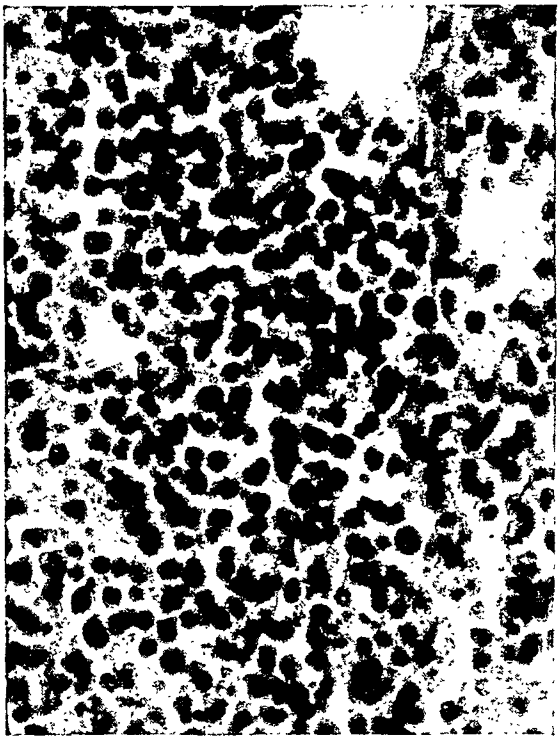

Fig. 4.—Section of bone marrow showing fatty marrow of femoral diaphysis replaced by very cellular erythromyelopoietic tissue. Many cells are myeloblasts and myelocytes. Smaller cells with black nuclei are normoblasts.

If it makes them more susceptible, then the question is, what is leukemia? How does this fit into the whole concept of leukemia? Leukemia is nothing more than a proliferation of the various cells normally present in the body, either as a result of the carcinogen effect of x-ray producing theis myeloproliferative disease, or, it may be a proliferative response to some insult to which the x-ray radiation has made the organ system susceptible. I like to think that this is what happened in this patient. Her resistance in the course of years, both as a result of the x-ray and the TEM therapy, was gradually reduced. The fact that she appeared chronically ill implies that before the clinical manifestations became obvious and before she came under observation, she had already been ill for some time. Then, having been made susceptible to the development of leukemia, she developed it terminally as a result of her granulocytopenia. She certainly became susceptible to gross bacterial infections. She developed a bacteremia as evidenced by both the urine and blood cultures. I would be surprised if she did not, in addition, have liver abscesses. She died in cardiac failure, probably with pulmonary edema. One interesting point is that in 1951, the basal metabolism and the I^{131} uptake were normal, but at the time we saw her, she had weight loss, increased oxygen demand, and a high blood uric acid level, indicative of an increased metabolic demand and rapid nucleoprotein turnover.

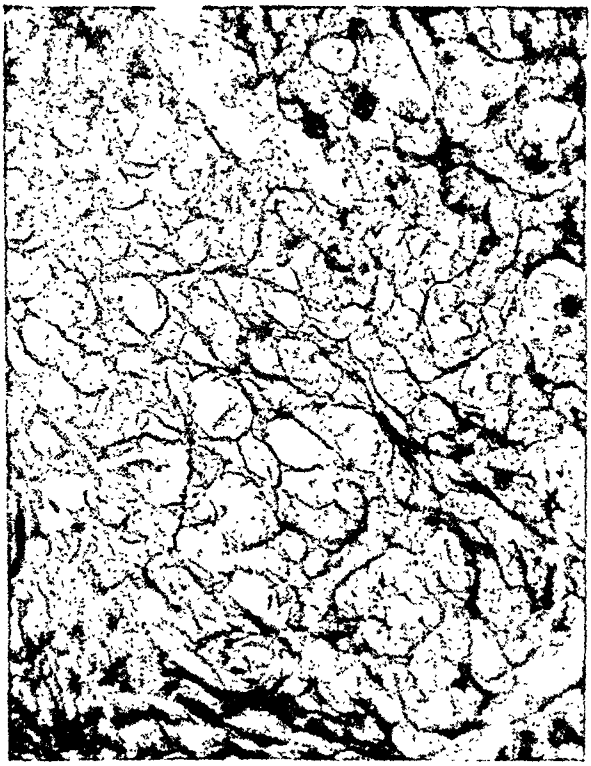

Fig. 5.—Section of bone marrow showing numerous reticulum fibers and collagen fibers.

Dr. S. Howard Armstrong, Jr.: Why did this patient die? Her hematological abnormalities hardly seem sufficient to explain the precise cause of death.

Dr. Schwartz: I think she died of cardiac failure and pulmonary edema, which I assume to be on the basis of myocardial failure secondary to the long duration of the illness, the moderately severe anemia, the increased metabolic demands of the underlying leukemia, and the terminal acute sepsis.

Dr. Armstrong: Could anything have been responsible other than what was defined bacteriologically? With regard to the isolation of staphylococci from the blood, in light of the skin lesions so suggestive of erythema nodosum, we can make three kinds of divisions. The fulminant coagulase-positive yellow staphylococci cause petechiae. These can go on to become white centered and resemble pyoderma, and the coagulase-negative staphylococci, which rarely cause septicemia, can produce a sort of granular erythema nodosum type of lesion from which staphylococci can be cultured early. Also, the hypoplastic kidney on one side, with a big kidney on the other, is a common observation in pyelonephritis. One must still dispose of the problem of a leukemoid response to severe infection.

Dr. Schwartz: The thing that prejudiced us against the purely bacteriological components of this case is that one of our group who saw the patient noted that she did not appear toxic, in spite of the severity of her illness. This suggested a terminal leukemia rather than infection.

Dr. Armstrong: This is important.

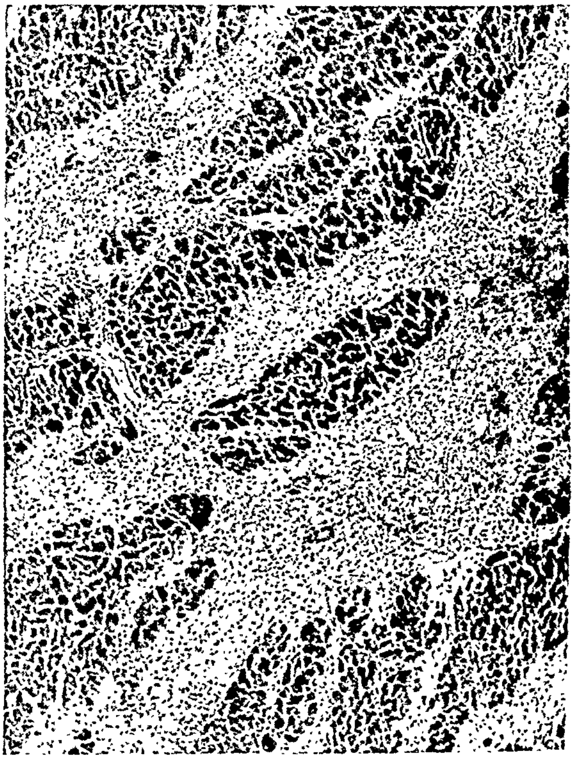

Fig. 6.—Section of myocardium showing infiltration by mononuclear cells belonging to myeloid series.

Dr. Harold Schoolman: What is the relationship of myelofibrosis to leukemia, and, could this patient have had this leukemia seven years before it became manifest?

Dr. Schwartz: With regard to the question of whether myelofibrosis antedates leukemia, in this patient the myelofibrosis was demonstrated first, so the answer is, yes, it can and did. This, however, must be modified by an explanation of what causes myelofibrosis, since we often see an acute leukemia in the so-called aplastic phase, which is similar to myelofibrosis. The second question is, could she have had the leukemia seven years ago. There is no evidence that she did. In the protocol, the marrow was described seven years ago as having a 1:1 ratio with no abnormal granulopoiesis, and I cannot interpret that, even in retrospect, as leukemia.

Question: Would it be pertinent that this patient complained of ankle pain and swelling and developed an area of exquisite tenderness and pain on the lateral aspect of the foot, beneath the lateral malleolus, and then responded dramatically to colchicine?

Dr. Schwartz: With a 9.1 mg. uric acid and a dramatic response to colchicine, in spite of the fact that this was in a woman, and in spite of the fact that she was 37 years old, I would have no quarrel with a diagnosis of secondary gout.

Clinical Diagnosis.—The final clinical diagnosis was acute granulocytic leukemia developing as a result of radiotherapy of a previous polycythemia vera and terminal staphylococcal pyelonephritis and septicemia.

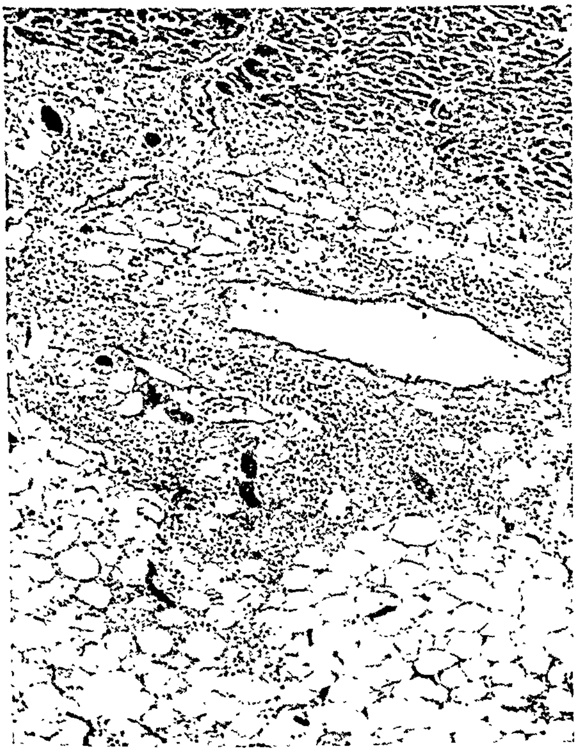

Fig. 7.—Section of subepicardial fat tissue showing infiltration by cells belonging to myeloid series.

Pathological Data

Dr. Paul B. Szanto: The body was that of a well-developed, somewhat emaciated woman. The pituitary was enlarged, as seen in multiparous women, due to increase in chromophobic and sparsely eosinophilic granulated cells of the anterior lobe. A moderately sized goiter (40 Gm.) was present. A mild peptic esophagitis was present which may have been responsible for the epigastric symptoms and signs. Corresponding with the history of "pus tubes," there was a bilateral hydrosalpinx. A confluent bronchopneumonia involved the lower lobes of both lungs. All cardiac chambers were dilated (weight 350 Gm.). Subepicardial hemorrhages were noted. Microscopically, the myocardium and epicardium showed cellular infiltration. The central nervous system showed some degenerative changes in the granular cell layer of the cerebellum, as seen occasionally in chronic alcoholism. The left kidney was hypoplastic and showed changes of a chronic pyelonephritis. The right kidney showed compensatory hyperplasia. Chronic pyelonephritis is frequently superimposed on a hypoplastic kidney.

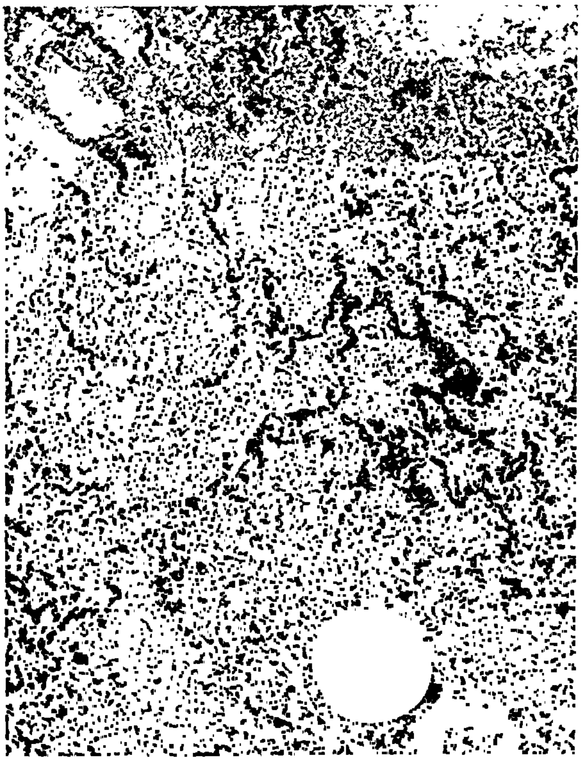

Fig. 8.—Section of lung; many cellular elements in alveoli are identified as myeloblasts and myelocytes.

The liver was enlarged (1,950 Gm.), and, on section, the lobular architecture was not discernible. Microscopically, the portal fields were moderately enlarged and cellular. The sinusoids were extensively infiltrated by mononuclear cells (fig. 1). Megakaryocytes were also prominent. Many of the mononuclear cells were myeloblasts and myelocytes. The hepatic changes alone permit the diagnosis of a recent exacerbation of a chronic granulocytic leukemia.

The spleen was large and firm (1,800 Gm.). The splenic tissue presented a homogenous appearance, and the follicles were obscured. In acute leukemia, the size of the spleen is usually around 300 to 400 Gm. In erythremia, as this case was originally diagnosed, the weight of the spleen is usually between 300 and 500 Gm. The large size of this spleen would suggest either agnogenic myeloid metaplasia or chronic granulocytic leukemia. Histologically, the architecture was obliterated. The Malpighian corpuscles were absent. This is important, because the absence of the follicles rules out the possibility of agnogenic myeloid metaplasia. This diagnosis had to be considered because erythremia may occur in the early phase of agnogenic metaplasia. In this case, microscopically, the splenic tissue was replaced by cells of fairly uniform cell types (fig. 2), myeloblasts and myelocytes intermingled with megakaryocytes (fig. 3). All lymph nodes were moderately enlarged, discreet, and on cut section gray-white and bulging above the level of the capsule. Microscopically, the normal architecture was obscured due to infiltration or replacement of the normal lymphoid tissue by cells of the myeloid series.

The bone marrow was very cellular (fig. 4), including the fatty marrow, which was replaced chiefly by myeloblasts and myelocytes, with distinct scattered megakaryocytes. In some areas of the bone marrow, just as in the biopsy specimen, fibrous replacement was seen. In these areas, numerous argentophilic reticulum fibers and collagen fibers were seen (fig. 5). The diagnosis of focal myelofibrosis of the bone marrow is confirmed. Iron pigment was completely absent in the bone marrow, liver, spleen, and lymph nodes. Some of the other organs also showed myeloid infiltrations. The spinal ganglia were infiltrated by cells of the myeloid series. The colon showed superficial ulcers with infiltration of the submucosa by cells belonging to the myeloid series, especially myeloblasts and myelocytes.

Returning to the heart, the infiltration of the myocardium (fig. 6) and subepicardial fat tissue (fig. 7) consisted of myeloblasts and myelocytes; thus, a leukemic infiltration of the myocardium resulted in cardiac dilatation. A closer examination of the lung revealed that most of the cells in the alveoli were myeloblasts and myelocytes (fig. 8).

Pathological Diagnosis.—The pathological diagnosis was chronic granulocytic leukemia with recent exacerbation, leukemic infiltrations of lymph nodes, spleen, liver, colon, myocardium, and lung, and focal myelofibrosis of bone marrow; bilateral confluent bronchopneumonia, lower lobes; peptic esophagitis; chronic pyelonephritis of the left kidney, and compensatory hyperplasia of the right kidney.

Comment

Dr. Szanto: Myelofibrosis or "myelophthisic" states may occur secondary to (1) irradiation, (2) chronic benzol poisoning, (3) carcinomatous metastasis leading to a desmoplastic reaction, (4) aplastic anemia, and (5) unknown causes. Myelofibrosis of any cause may lead to myeloid metaplasia in the various organs, especially the spleen. The so-called agnogenic myeloid metaplasia (chronic nonleukemic myelosis)[1] is characterized by a progressive hepatosplenomegaly, with preservation of the Malpighian corpuscles, and it may or may not be associated with myelofibrosis. As mentioned above, in this case, the Malpighian corpuscles were absent, and the architecture of the spleen was completely obliterated. It should be pointed out that in our experience most of the cases diagnosed as agnogenic myeloid metaplasia are atypical forms of chronic granulocytic leukemia. In this case, none of the causes enumerated above were present to explain the myelofibrosis.

This 37-year-old woman developed clinical and hematological findings, interpreted six years prior to her death as erythremia. Although the possibility exists that polycythemic blood findings (erythrocytosis, but no true erythremia) may develop in the early phase of an agnogenic metaplasia, a review of the original symptoms makes the diagnosis of erythremia (polycythemia vera) acceptable. In the subsequent two years after the diagnosis of polycythemia vera was made, the patient received energetic treatment consisting of numerous phlebotomies and radiation. Later she developed moderate anemia, leukopenia, and a hypocellular bone marrow, findings which may reflect the myelofibrotic changes in the bone marrow. In the last months of her life, she developed an acute exacerbation of a chronic granulocytic leukemia.[2] We agree that the joint pains were manifestations of a secondary gout as occurs in leukemia. The marked orthopnea may be related to the extensive leukemic infiltration of the lungs. Myelofibrosis and myelosclerosis may develop in the course of leukemia. In leukemia, as well as in erythremia,[3] the leukemic process may lead to an increased activity of the fibroblasts and/or osteoblasts, or it may simulate the differentiation of the mesenchymal cells of the bone marrow into fibroblasts or osteoblasts.

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3. Wasserman, L. R.: Polycythemia Vera—Its Course and Treatment: Relation to Myeloid Metaplasia and Leukemia, Bull. New York Acad. Med. **30:**343-375 (May) 1954.

"All the comforts of home" is no cliché in a modern nursing home where couples may share their declining years in comfortable surroundings. Medical supervision and skilled nursing care play a key role here (see "Nobody Calls This an Institution," page 146.

MEDICINE AT WORK

- *Nursing Homes Roundup*
- *Secrets Not to Keep*
- *War on Staphylococcus*
- *Prescription Against Quackery*
- *'Village' for Oldsters*
- *Quotes from Minneapolis*
- *Where the Aged Don't Worry*

Sunrise and Sunset

Concern for infants matched concern for oldsters in the science-socioeconomics area which confronted the A. M. A. House of Delegates in Minneapolis last month. This is what the Committee on Maternal and Child Care announced as a goal:

> The objective of perinatal mortality and morbidity studies is to improve the production of normal human beings. The elimination of deaths and damage during the process of reproduction is the ideal for which we should strive.

And this is from Governor Orville L. Freeman of Minnesota:

> Can you help us to find a way to apply the voluntary health insurance principle to elderly and retired people? Can you help us to develop a program, that is within our means, to provide the kind of preventive care and attention that will make the sunset years healthier and happier? The people feel this need and when they feel it badly enough, they demand that it be met. The people then say, "there ought to be a law." Yet the best solution is seldom reached in an atmosphere of urgent need or bitter controversy.

On both of these challenges, the House took definitive action, adopting the Committee report as well as a far-seeing program for the aged.

For other selected quotes from the Clinical Meeting in Minneapolis Dec. 2 to 4, see page 150 of this section. A series of Medicine at Work reports and photos relating to facilities for the aged begins on this page.

What Is a Nursing Home?

Society Searches for an Answer as Facilities for the Aged Boom

"The term 'nursing home' has been used so indiscriminately that it has almost ceased to have any meaning." This statement, made a few years back by the director of an agency for the chronically ill, outlines the situation involving nursing homes today which is ambiguous: people talk a good deal about nursing homes, but often they are not talking about the same thing.

The Public Health Service, in a monograph called "Nursing Homes, Their Patients, and Their Care," underlines this national confusion. It states:

> As a relatively new type of facility, the nursing home is not yet clearly conceived and understood. Like most newly emerging social institutions, it was not established full-blown and definitive; it has found its way gradually, hesitantly, and to a great extent, expediently. What it offers therefore is not necessarily always the professionally appropriate answers to the problems it attempts to meet, but rather responses dictated by immediate practicalities. It is not a homogenous type of institution; it means different things in different localities or to different people.

But lack of a proper definition has done little to dampen the growth of nursing homes in this country. Though their number was insignificant in the Thirties, a detailed survey made in 1953-'54 disclosed a national total of 25,000 establishments that qualified as nursing homes under the generous working definitions used in the PHS study.

Whatever their other variations, those homes surveyed by PHS were in agreement on one thing at least: they catered almost exclusively to the needs of the aged. Figures show the average age of the patients to be 80. Fewer than one-tenth of the residents of these homes are less than 65. As might be expected in this age grouping, women outnumber the men two to one.

Medical or Social Need?

Nursing homes are an outgrowth of our modern society with its highly complex social, medical, and economic structure. They have been created to fill a need that may be almost as much social as medical. Their function in the modern scheme appears to be poorly understood by the public.

These homes occupy a position in the medical care spectrum between the home for the aged and the chronic disease hospital, with overlaps at each end. Some have highly organized medical direction and offer housing almost as an adjunct. Many others are primarily shelters that operate without even the benefit of a trained practical nurse. They come in all sizes, too. While more than four-fifths of the 25,000 listed by PHS were proprietary, these accounted for less than half the total number of beds. The other half were in homes operated by voluntary organizations or governmental units.

Such a burgeoning area of medical care could not be long ignored by those interested in the health of the nation's oldsters. Attempts to develop standards for such homes are being or have been made by the American Medical Association, the American Hospital Association, the Public Health Service, and the American Nursing Home Association. Last November, the AHA announced it was prepared to inaugurate a program "to list inpatient care institutions other than hospitals as nursing homes." An attempt to correlate the resources of the principal purveyors of health care for the elderly has been undertaken by the Joint Council to Improve the Health Care of the Aged. Formed last year, the group's membership includes representatives of the A. M. A., ANHA, AHA, and the American Dental Association. They have labored tirelessly to bring about a solution to this broad and complex problem.

Definition by Function

Although their practices differ widely, nursing homes have been categorized by the Public Health Service in three classifications—one with two subdivisions:

Skilled Nursing Homes. Those capable of offering procedures, employed in caring for the sick, which require some technical nursing skill beyond that which the untrained person can administer.

Personal Care Homes. Those offering primarily such personal services as help in walking, getting in and out of bed, bathing, diet supervision, and aid with self-administered medications.

Sheltered Homes. Those offering room, board, custodial services, laundry, and minor personal services.

It soon became apparent that personal care homes were of two distinct types: those that offered personal care only, and those that had the personnel and equipment to offer skilled nursing services to a portion of the residents.

A current effort by the Public Health Service to identify various types of facilities by means of a numbering system came in for sharp discussion last month when the A. M. A. was host to officials of PHS, AHA, and ANHA at a meeting in Chicago. Purpose of the proposed numbered categorization would be to aid states' attempts at licensure.

In its current effort to study and develop data on nursing homes, the A. M. A.'s Committee on Medical and Related Facilities of the Council on Medical Service sent inspection teams to 35 geographically separated nursing homes last summer. Places chosen were considered to be among the nation's best.

For examples of two of the 35, see "Village for the Aged" on Page 149 and "Nobody Calls This an Institution" on Page 146

Preliminary reports of inspection teams indicated a variety of conditions in these homes. One stated: "There have been a few homes where the medical staff set-up, on paper, looked like the answer to a patient's prayer. Then you find that the medical director is in, perhaps, at the most once a week, and that the majority of medical supervision is handled by nurses."

Other inspections in the series pointed up a certain lack of agreement as to what constitutes proper social and rehabilitative programming in these homes. In some, the visitors found physical and

Yellow-Page Puzzle

The pages of a classified telephone directory in just one U.S. metropolis lists 149 establishments under the heading "Nursing Homes," yet the advertisements for these same homes indicate how their functions vary.

One, calling itself a convalescent home, offers "hospital care." Another, managed by a practical nurse, also caters to convalescents—and the elderly retired. Some advertise that they accept "mental cases," but they usually stress the adjective "mild." Others exclude "mental cases or alcoholics.'

The nursing home classification also states: (see also Sanitariums). A look at the listings for sanitariums shows duplicate listings for many of the establishments also classified as nursing homes.

The phone book of another large city lists a *similar array under the catch-all title of nursing* homes, yet one of its offerings advertises itself as a "hotel for senior citizens—not a convalescent home." That place does, however, have "complete medical services available."

occupational therapy programs going full tilt with the approval of the residents. In others, such services were largely unused because the staff had been unable to interest the patients in participation. Indeed, in one home, the administrator questioned the value of occupational therapy as a morale builder, and avoided it as a matter of policy.

Is Money the Root?

Money—or, to be more accurate, its absence—often lies behind some of the more obvious faults of nursing homes. Dr. Willard Wright, chairman of the A. M. A. Committee on Medical and Related Facilities, says: "Increasing numbers of persons are dependent on various forms of governmental assistance. Frequently it is in this area that operators of nursing homes find themselves held down to such low income that they are unable to provide the best type of services."

This problem is greatest in those states where an indigent care program is not available. And yet, some homes—such as Mary Manning Walsh in New York, and Good Samaritan Village in Hastings, Neb. —operate successfully in spite of this handicap.

Medical care in the homes visited by the A. M. A. teams varied widely, yet staff men making the inspections found that the effectiveness of such care and supervision depended far more on the interest and effort of those taking part than on the plan itself. They found that many of the larger and newer homes had one or more full or part-time staff physicians who handled almost all the day-to-day medical care in the home, as well as responsibility for general medical policies. The other extreme was represented by small homes which had no staff physician, but engaged in various kinds of working relationships with local doctors, many of whom had their own patients in the home.

"In these latter cases," an interim A. M. A. report states, "one of the local physicians often acts as a confidant or advisor to the nursing home administrator on general medical problems. This type of arrangement is usually as informal as picking up a telephone, but depending on the attitude of the physician and administrator, has proved completely adequate for insuring good medical policies."

The physical plants of these homes vary almost as widely as do the administrative policies that guide them. Many of the smaller ones inhabit large homes dating back to an earlier era which offer stately surroundings often ill-suited to the needs they are expected to satisfy. With less than half their patients ambulatory, and a large proportion mentally disoriented at least part of the time, nursing homes have some important safety problems to consider and overcome. They are not always successful, as was violently illustrated a few years ago when 70 patients were incinerated in a Midwestern home as fire razed their quarters.

Chairman of the A. M. A. Committee on Medical and Related Facilities of the Council on Medical Service is Dr. Willard Wright of Williston, N. D. Other members are Drs. William F. Costello of Dover, N. J.; Robert L. Novy of Detroit; David Henry Poer of Atlanta; W. C. Stover of Boonville, Ind.; Walter E. Vest of Huntington, W. Va.; and John M. Rumsey of San Diego, Calif. Dr. Edward C. Rosenow of Los Angeles is a consultant to the Committee. Staff Secretary is Mr. George W. Cooley.

Other homes have been formed in more suitable, though unorthodox, facilities. Some have been constructed for the express purpose of housing a nursing home, but these appear to be the fortunate minority. More often they occupy quarters constructed for purposes now outdated: a school, a housing project, a former hospital.

Interest Quickening

Interest in the field of aging is on the upswing. Not only are nursing homes and similar facilities burgeoning, but public and professional concern with the problems of the elderly becomes more apparent daily. Within the past decade, giant strides have been made in this field. All states now have licensure laws covering nursing homes. The ANHA (grown to 4,500 members from a mere handful in 1954) works valiantly with other interested health groups to develop standards. In addition, the ANHA spends much of its time on educational programs for home operators.

The answer to all of this renewed interest is probably manifold: The obvious reason lies in the actuarial tables which show ever-increasing numbers reaching and surpassing the historic three-score-and-ten. A less obvious answer, but perhaps an even more pertinent one, was advanced last year by Dr. Cecil Wittson, a psychiatrist who is a member of the A. M. A. Committee on Aging. Speaking in Chicago before the A. M. A. Planning Conference on Aging, Dr. Wittson told the assembled physicians:

"Careful research over the past 2,000 years has finally established that senility has an incidence of 100 per cent among living populations. Geriattrition is the common fate of man. For once, the healthy future you are attempting to guarantee is not the other fellow's—it is your own."

Being dependent on a wheelchair doesn't mean inactivity for residents of the Mary Manning Walsh nursing home. Games and sports add interest and therapeutic opportunities to the home's daily schedule.

Nobody Calls This an Institution

Folks at Mary Manning Walsh Home Haven't Time to Worry About Old Age

There was concern, but no panic, when one of the aged male residents of the Mary Manning Walsh home on Manhattan's 59th Street failed to show up for lunch. Police were alerted and the Sisters scoured the neighborhood, but, even at dinner time, no trace could be found of the errant guest. It was late in the evening when he finally returned, tired but happy after a long day—spent at a Long Island race track.

In many nursing homes, the incident might have been the signal for a tightening of restrictions on the home's residents, but at Mary Manning Walsh, operated by the Carmelite Sisters, Mother Bernadette views such occurrences as a natural by-product of a policy that encourages all the activity, interests, and cosmopolitanism any resident finds himself capable of.

In a "constantly adapting" policy of administration, Mother Bernadette has come up with some happy solutions for some old problems:

For a retired milliner finding it difficult to adjust to the new life—a basement hat shop that serves the dual purpose of keeping her happily busy, and providing new bonnets for the home's feminine residents.

For those liking a nip or two but finding the local tavern too much of a good thing—the Emerald Room, a bar, complete with a red-jacketed, brass-buttoned bartender, that opens daily at 4 p. m. and serves cocktails for a "donation," a system which obviates the need for a liquor license.

For residents who want to feel they have a part in the operating decisions of the home—a resident council that weighs submitted ideas carefully, transmitting the best to a usually amenable administrator.

Hotel for the Elderly

Although Mary Manning Walsh home is an "institution" by definition, it has few of the undesirable attributes commonly associated with the term. A home for more than 300 persons, chiefly women, it occupies three interconnected buildings that formerly housed the New York Orthopedic Hospital. Operated on a nonprofit basis by the Roman Catholic Archdiocese of New York, the home offers several grades of care for the aged on a hotel-like basis. Open to all, regardless of race or religion, it is governed by a nine-man board that includes physicians, businessmen, lawyers, a Cardinal, and others. Couples, as well as individuals, are accepted. Female residents outnumber the males by about 5 to 1.

Medicine's role in the seven year history of Mary Manning Walsh home has been a constant one. Indeed, its medical problems were carefully considered by physicians before the home was opened. Dr. Howard Rusk, director of the Institute of Physical Medicine and Rehabilitation of New York University–Bellevue Medical Center, provided guidance in the early days and has continued his interest as a member of the home's board of directors. Dr. John F. Maloney, medical director for the home, supervises all medical care and matters of medical policy. Other staff physicians include Drs. Michael Dasco, Ann Maloney, and John Sokolow, who are retained on a part-time, paid basis. In addition, a number of the city's medical specialists act as consultants when needed.

The resident arrives at the home with a medical

> If Mary Manning Walsh home had a formal slogan, it would probably be "The Residents Come First." Facilities and programs are in a constant state of flux as Mother Bernadette works to better her home's services. She says:
>
> *"We don't want to modify the living habits of the residents any more than is absolutely necessary. We try to make Mary Manning Walsh as much like the homes they came from as possible. If they've been used to a drink before dinner, a snack between meals, or smoking a pipe, we want them to continue to do so here. Our convenience is secondary to their happiness."*

history and referral sheet filled out by his physician. Within 24 hours, he is given a physical examination by a member of the medical staff. Medical care during residence is based on the individual's condition, but the emphasis is on rehabilitative procedures for those suffering from illness or disability. Residents may have their own physicians, but staff doctors make a daily check on the condition of those needing skilled nursing care.

No Time for Self-Pity

The range of activities open to residents is extensive. In addition to the usual therapeutic arts and crafts, a resident may help plan and write a bimonthy newspaper, take photographs, act in or direct one of the many plays or shows, play the piano, sing with a choral group, take a course in music appreciation (or teach it), go for a boat ride around Manhattan, spend a few hours on a picnic, get a permanent or a haircut, entertain visitors in the snack bar, play games, or just read, chat, or meditate as the spirit moves.

Parties and special occasions are celebrated in constant succession at Mary Manning Walsh. Wedding anniversaries, birthdays, and legal and religious holidays all come in for special attention. In the summer, the buildings' balconies and roofs are used for exercise and entertainment, and, in cooler weather, the home's auditorium often is the scene for shows put on by visiting entertainers, many of them performers at one of the city's larger night clubs whose owner is interested in the home.

The majority of the home's residents are in their eighties. Most of them suffer from some handicap, many are bedfast or in wheelchairs. Yet some of them manage a surprising amount of activity:

—One woman won quite a TV following on a show featuring the aged.

—A male member of the home used his age to good advantage when he appeared as the model, complete with tattoo, in a national advertising campaign for a cigarette company.

—An architect, living in the home with his wife, still works as a consultant in his profession.

Beds and Wheelchairs, Too

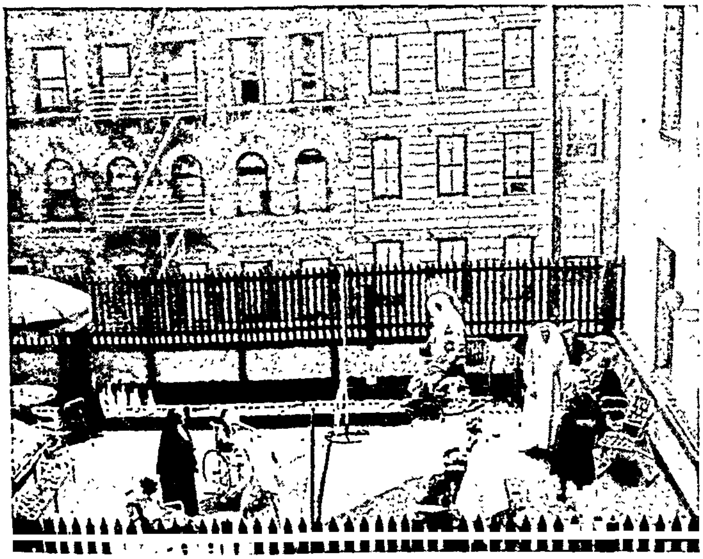
While the more active residents provide for their own interests, the less fortunate are not forgotten. Bedfast patients, in addition to expert nursing care, are given small attentions too. A supply of pretty gowns and bedjackets are liberally used, and shampoos and hair grooming are offered as needed. For those confined to wheelchairs, a variety of therapeutic activities is maintained, even such unlikely ones as bowling and badminton.

Some of the home's residents are dependent on public assistance; others are provided for through their own resources or those of relatives. The administrator says the home is self-sustaining, partly due to the fact that many of the staff are members of the religious order. Groups of nursing aides are assigned to the home for two-month training periods.

Mary Manning Walsh home gives every appearance of being almost an unqualified success—and appearances, in this case, are not deceiving if you listen to one of the home's first residents. A retired physician, Dr. Francis A. Schneider, on the occasion of the home's fifth anniversary, wrote:

"Five years and three months have rushed by . . . never wondering what to do with ourselves, never lonesome, but always occupied wishing the day would take on additional hours. My roommate (alias wife) has so many interests that I fear our relationship might be reduced before long to a mere bowing acquaintance from a distance. As for myself, I have widened my horizon in knowledge, hobbies and experience to such an extent that an enumeration of them before our entrance [to the home] would have sounded ludicrous."

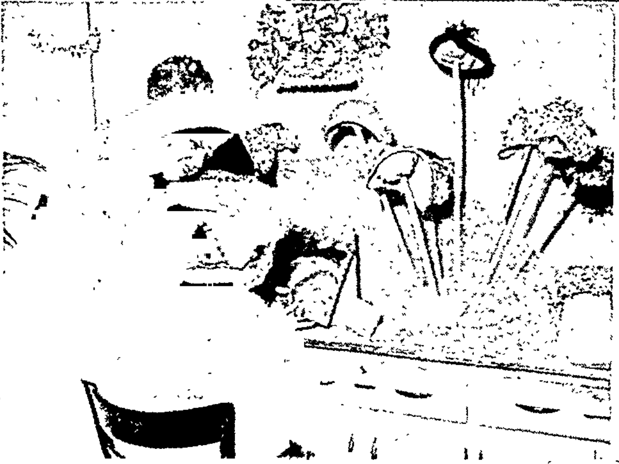
Routine Medical—
One of many check-ups



No Miracle on 59th Street—
Just a happy home amid tenements

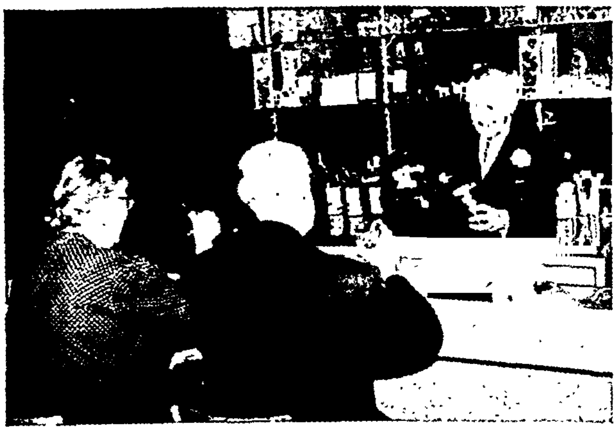
On this and the preceding page are scenes from the Mary Manning Walsh home on 59th street in Manhattan. While medical care is a key factor in this nursing home that "nobody calls an institution," a myriad of other important aspects are called into play—a millinery shop, a bar, bowling, arts and crafts.

Easy Does It—
Rehabilitation in action



How Perky—
The millinery shop

Keeping Busy—
Everybody works at something



An Aperitif—
The bartender lives here, too

'Village' for the Aged

Nebraska Unit Emphasizes Medical Care at Every Level of Need

People never grew old in Sir James M. Barrie's "land of never-never," and it might be argued that this has practical as well as theoretical advantages. For one thing, its citizens did not need to worry about such matters as pensions and social security.

But in Nebraska—just as in the rest of the world—aging has its problems, and it is here that a "village" devoted to the needs of the elderly is growing. Opened to residents only eight months ago, it had nearly 200 admissions last year.

Good Samaritan Village is geared to the requirements of the aged whether they may be retired couples able to care for themselves or bedridden patients without home or family. Sponsored and originally financed by the Good Samaritan Society, a Lutheran church-related group which operates 60 nursing and old age homes, the Village was founded in a wartime housing development known as Spencer Park, an outlying section of Hastings. Although a community unit in its own right, the "village" has no civic government of its own.

It was established in 1957 with the purchase of about half of the project's 850 apartments. An option was taken on the other half, and the Society is currently awaiting a decision on its application for a $425,000 FHA-insured loan. Streets and sidewalks are paved, and all apartments are equipped with gas radiant heating units and water heaters.

Rev. William Goldbeck, an ordained Lutheran minister, became administrator of the 80-acre Village after serving as chaplain at the nearby Hastings State Hospital. He is aided by an advisory committee made up of the business and professional leaders of Hastings. Other volunteer groups help out with recreational ventures.

Plan for Medical Care

A local physician interested in geriatrics, Dr. Gerald Kuehn, acts as medical director of the rest home and infirmary. Recommended by the Adams County Medical Society, he supervises the over-all medical program, acts as physician to those who have none, and is available in emergencies. Many residents make their own arrangements with private physicians, as do some of the infirmary patients.

Hospital care is available to Good Samaritan Village residents at the 138-bed general hospital in Hastings, a short drive away. Laboratory work is currently done through outside facilities, but an enlarged infirmary now in the planning stage will include a laboratory as well as facilities for oxygen, basal metabolism rate equipment, electrocardiogram, x-ray, and sterilization.

The Village is designed to operate on a nonprofit, self-sustaining basis offering "security, Christian care, and companionship" for those of normal retiring age or who for other reasons must limit their activities. Five levels of care are available:

—One to three-bedroom apartments for couples or individuals who are capable of caring for themselves, and who seek only the companionship of others of their age group.

—Similar apartments for those who can maintain their own households with assistance from a "house visitor" who will come each day to help with household duties and meal planning.

—The same living arrangements as above, but with provision for one or more meals in a central dining room.

—A rest home providing personal care under medical supervision for those who need help with feeding, dressing, walking, and similar activities.

—An infirmary section of the rest home for those in need of nursing care and medical supervision.

Apartments consist of a kitchen, living room, and from one to three bedrooms each. Monthly rental is $25, $30, or $35—depending on the number of bedrooms. Cost of gas and electricity is extra. For those found to require it, the "house visitor" will drop in at no extra charge. There is an extra cost for meals eaten in the central dining room.

Care in the rest home includes meals, laundry, and room service. For the patient up and about, the cost is $85 to $95 a month. Cost for the person in a wheelchair or walker is $100 to $125. Bed care in the infirmary is available for $125 to $150 a month. An expected innovation will be suites for couples in the rest home, each with a private bath.

Population Possibilities

First occupants of the Village moved in last summer. At last report, only a handful of the apartments had been rented, but the existing infirmary was filled to its capacity of 11 patients. Additional construction underway will increase capacity to 52 this spring. The rest home is also in its infancy but will be able to accept 92 residents on completion. Eventual population of the Village may reach 800 or more, if all available housing is used. Residents furnish their own apartments—a point which, it is hoped, will help to make them feel at home.

Plans for the future at Good Samaritan Village are hopefully farsighted. Additions to the physical plant will include a shopping center, chapel, recreation center, park, greenhouse, library, and hobby shop. Due for increasing emphasis are social services and rehabilitation programs.

While the land of Peter Pan has not lost its appeal to our imaginations, it is well to view aging in a more pragmatic light. Answers to the problem of caring for the elderly are eagerly sought today, and Good Samaritan Village is convinced it has one of the better solutions.

They Said It at Minneapolis . . .

Some significant comments reported "on the record" at the 12th Clinical Meeting last month:

Unfortunately, many people who habitually advocate government solutions to health problems do so on the basis of political expediency. Some of them, including well-intentioned physicians, support such programs because of the motives and objectives involved, but they choose to ignore or minimize the great dangers inherent in the means. As a result the medical profession frequently is forced into opposing legislation which has a worthy goal, but which offers numerous pitfalls for both medicine and the public.

We should make our views known—in community affairs, on national issues, on any and all questions of the day. There is a direct relationship between the future of individualism and the ultimate fate of the medical profession.

In our relations with third parties we cannot deny the validity of criticism. We should welcome it, study it and learn from it. . . .We also should appraise some of our own programs—among them, the effectiveness of our policing of that minority of physicians whose actions bring discredit and trouble to all of us. . . .A critic of the schools is no more automatically an enemy of education than a music credit is an enemy of music. By the same token, a sincere critic of bad medicine can be the best kind of friend for good medicine.

—Dr. Gunnar Gundersen, President of the A.M.A.

In recent years medicine may have suffered more from its successes than from its failures. Progress in postponing death has come so rapidly in the past several decades that we must now recognize that the rate of progress can scarcely be continued at its frenzied pace.

—Committee to Study A.M.A. Objectives and Basic Programs.

Not only are the ladies [of the Woman's Auxiliary] a charming, indispensable, stimulating part of our everyday lives, aiding most in preventing us from regarding our professional work as a chore, but they also play a very vital part in Medicine in our country.

—Report adopted by House of Delegates.

There are approximately 1,500 companies in the health insurance field, and the character of the industry is such that the whole industry tends to follow, with comparable plans, once a few enter into a new phase of underwriting. Since some of the major companies are already active in provision of (1) coverage for an individual or for group enrollment for individuals over 65 and their families, and (2) "Paid-up" coverage at retirement, a rapid growth in such types of contracts may be expected in the future.

—Adopted report of Council on Medical Service.

It seems reasonable to assume that underwriting organizations, as well as health and welfare fund administrators, individuals and physicians need to understand the relative values of physicians' services if health insurance and similar mechanisms are to succeed and fulfill their potential in financing, either in full or in part, the cost incident to medical care.

—Committee on Medical Practices.

Of the 15 bills of a medical nature enacted into law by the 85th Congress, only one was opposed by the A.M.A. . . . In its statements to Congress the Association was supporting the legislation or principle involved on 19 occasions and was in opposition on only six occasions. We believe that these facts should be publicized to the American public and to the medical profession in order to help eliminate the oft-heard charge that the Association is basically negative in its approach to legislative matters.

—Report adopted by House of Delegates.

Whatever progress is to be achieved in the future cannot be made by unilateral action—whether by the medical profession or "third parties" in matters which intimately concern both groups. Problems and issues which have disturbed relationships in the past must be resolved on the basis of a mutual acceptance of responsibility, an understanding of the professional relationships and patient care involved, and other social and economic factors.

—Council on Medical Service.

A.M.A.'s House of Delegates, like the Congress, carries on its business openly. Our proceedings are of interest to both the profession and the public. Under these circumstances the failure to disseminate information regarding an important policy matter only stimulates rumor and misrepresentation. In the long run it is to our advantage, as well as the public and the profession, to make available factual, judiciously selected, information on matters under consideration as well as on those on which definitive action already has been taken.

—Adopted report of Board of Trustees.

War on Staphylococcus—Via New Training Aids Program

Spurred by the appearance of antibiotic-resistant Staphylococcus pyogenes var. aureus, a multiagency committee is bolstering the national program aimed at control of this bacterium in hospitals.

Known as the Interagency Committee for Training Aids on Staphylococcal Disease, the group was created through the efforts of six major health organizations: American Academy of Pediatrics, American College of Surgeons, American Hospital Association, American Medical Association, American Nurses Association, and the Communicable Disease Center of the U. S. Department of Health, Education, and Welfare.

An exchange of information on audiovisual and other training materials will be the aim of the new group. Mr. Ralph P. Creer, Director of Medical Motion Pictures and Television for the A. M. A., is chairman. The committee plans an immediate review of all existing training aids and will coordinate production, distribution, and utilization of future audiovisual materials.

The committee also hopes to avoid duplication of training aids and to encourage presentations that will best orient both professional and subprofessional groups to the increasing challenge posed by the Staphylococcus problem.

Prescription Against Quackery Written by A.M.A. Bureau

The letter came to the A. M. A. Bureau of Investigation from a physician faced with a dilemma as old as quackery itself:

> I have a young child as my patient. She has carcinoma of inoperable type. Relatives are trying to persuade the father to send her to Dallas for the Hoxsey treatment. My arguments against this would carry more weight if you could supply me with material regarding this treatment. Please send whatever information you have available.

The Bureau, in its report to the House of Delegates last month, noted that in the past year it had answered 3,200 similar inquiries. Some are from physicians; many more are from students, government agencies, Better Business Bureaus, and just plain hopeful, but slightly suspicious, laymen.

The Bureau's half-million index cards, carefully catalogued, provide a running history of modern charlatanry, a monument to man's gullibility in medical matters. But man need not be ignorant of the facts on "new" nostrums, machines, or treatments purported to relieve all the ills of mankind. The accumulated knowledge of the Bureau is available to both physicians and the public for the cost of a 4-cent stamp.

What sort of questions do they have, these correspondents? They vary from queries on the therapeutic qualities of garlic pills to the efficacy of vibrating mattresses as reducing aids, from hair growers to bust developers. There are trends, however, usually tied closely to diseases that have been heavily publicized.

Foremost among these for the past several years has been cancer, although the tempo has been falling off. Cancer questions reached a peak of more than 1,000 in 1955, but since then an increasing campaign in public education, effective enforcement of the Food and Drug Act, the death of two cancer quacks, and the closing of a Missouri "institute" have slowed the stream.

Other popular subjects of late have been alleged "rejuvenators" (especially Royal Jelly), vitamin preparations, reducing aids, and the many gadgets of the ingenious quack.

The Bureau—headed by Mr. Oliver Field, an attorney with a background of investigative experience—cooperates closely with law enforcement agencies, offering information on request and adding data from these agencies to Bureau files where applicable. The federal Food and Drug Administration, the Post Office Department, and the Federal Trade Commission are no strangers to Field. Often the Bureau's files have been helpful to them as source material for their investigations.

In addition to answering mailed queries, Field makes an average of 50 talks a year before medical societies, civic clubs, PTA's, service organizations, and university groups. Field agrees only partially with Voltaire's opinion that "the charlatan was born when the first knave met the first fool." He believes that it is not the foolish but the ignorant or misinformed who are the ready victims of quackery.

Secrets Which Doctors Should Not Keep

More than one petty thief has hit the big time at a doctor's expense—and there is some evidence that the apathy of the victim may be giving such a criminal a push up the ladder of "success." The following selected recent newspaper accounts indicate a rising trend of stealing from physicians:

—Late last summer, the Associated Press reported the case of Joseph Richard Gerard, who took $9,500 in cash and $12,420 in checks and securities from a safe in the home of a physician "friend" in New Athens, Ill. Gerard spent three months traveling and gambling in an attempt to get money to repay the doctor. Conscience-stricken, he finally gave himself up in San Antonio. According to the news report, "Mystified local authorities said the doctor had not reported the theft to them."

—Other thieves thrived on their victim's hesitancy to discuss his affairs last year, when $245,000 in stocks were stolen from a Lancaster, Pa., retired physician. According to the *New York Times*, 82-year-old Dr. Donald M. Myers returned from town one night to find three men waiting for him. They escorted him inside his home, tied him up, and broke open his desk. There they found 22,313 shares of stock. Dr. Myers freed himself after the robbers left, but it was not until 10 days later that he told a friend—and swore him to secrecy.

"It might have remained a general secret," the *Times* reported. But two months later a man assumed the identity of the aged doctor and tried to sell the securities to a brokerage firm, which became suspicious and found out they had been stolen.

—According to the *A.M.A. News*, two "patients," working separately, made a healthy profit on the principle that doctors also have neither the time nor the inclination to check up on bank accounts.

The A.M.A. Bureau of Investigation is working with police by alerting the profession to operations of such bogus check passers and other swindlers. Oliver Field, director of the Bureau, says:

"Swindlers and thieves are free to steal again whenever their victims keep silent. Physicians, particularly, have a duty to protect fellow practitioners, as well as all fellow citizens, by reporting such crimes immediately to police."

THE JOURNAL
OF THE AMERICAN MEDICAL ASSOCIATION

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SMALLPOX TODAY

VIVID impressions have been recorded by Prof. A. Herrlich of a severe smallpox epidemic that began in East Pakistan and came to involve India. Herrlich was permitted by the Public Health Service in Bombay to spend four weeks at the City Fever Hospital, where he was able to examine more than 500 smallpox patients. He returned to Germany with much valuable material, including continuously refrigerated specimens of blood and tissues. The rapid progress of virology in recent years and the reports of new methods for cultivating the smallpox virus enhance the value of such material.[1] In addition, Herrlich has published photographs that strikingly illustrate the course of smallpox in its severe forms.[2] These should be of special interest to physicians in countries like the United States, where "classical" smallpox is absent and the diagnosis of cases made mild by vaccination has become difficult.[3]

The cases seen by Herrlich were of the worst kind. He saw more than one patient whose head seemed to be covered by a single confluent lesion, with mouth and nose so obstructed by swollen tissues and purulent discharges that the drinking of water became impossible, tracheotomy was out of the question, and asphyxia could only be postponed by giving oxygen through a nasal catheter. He saw patients lying practically immobilized in an armor of crusts that covered pus, blood, and indurated tissue. In one patient who recovered, the process of desquamation included the shedding of the soles of both feet.

At the height of the outbreak in Bombay there were 450 smallpox patients at this hospital, many of them sheltered in large emergency tents and cared for partly by relatives and friends. The picture is worth keeping in mind, for the adequacy of our medical, nursing, and hospital facilities in the face of possible epidemics of this magnitude needs to be reviewed from time to time. Herrlich pays tribute to the untiring efforts of the young Indian physicians and nurses, overwhelmed as they were by this encounter with a disease for which there is still no direct remedy. There was also a shortage of antibiotics. They do not prevent the multiplication of the smallpox virus but they are important in controlling secondary infections. The incidence of such infections—abscesses, secondary pneumonia, orchitis, osteomyelitis, and others—was alarmingly high. It might well have been reduced had it been possible to use antibiotics on a larger scale.

Smallpox is still endemic in some parts of the world and is still being carried about by international travelers. The World Health Organization has reported[4] that no less than 18 countries were thus infected with smallpox in the year 1956. The disease was successfully localized in 10 countries, but epidemics started in 8. In 1956 WHO stated[5] that "for the past 5 years 58% of all cases were reported from India and Pakistan." It was further stated that "The Indian sub-continent (India and Pakistan) is at present the principal endemic reservoir of variola major, with high mortality. Vaccination and previous attacks have not yet built up a sufficient proportion of protected population."[6] In 1958 WHO reported, further, that the incidence of smallpox in India was rising.[7] It appears that these were the signs presaging the "smallpox year" that Herrlich witnessed.

People who have never seen smallpox may find it hard to maintain that feeling of conviction that is needed to run a continuous program of vaccination. On this point Herrlich, who is director of the Bavarian State Vaccination Institute writes with emphasis: "The only way to combat smallpox is to vaccinate, and the only way to avoid the complications of vaccination would be not to vaccinate. But in all our discussions of the advantages and disadvantages of vaccination we should not belittle the importance of smallpox as a disease . . . It continues to defy the exertions of physicians and remains as treacherous as it was in the days of the Arabs who first described it."

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[1] Cultivation of Smallpox Virus, Foreign Letters, J. A. M. A. **163:** 762 (March 2) 1957.

[2] Herrlich, A.: Variola, Deutsche med. Wchnschr. **83:**1426-1428, 1436, and 1441 (Aug. 22) 1958.

[3] Americas, in Gear, H. S.: Disease Control and International Travel: Review of International Sanitary Regulations, Chron. World Health Organ. **10:**300 (Sept.-Oct.) 1956.

[4] Smallpox Spread by International Travelers, Medical News, J. A. M. A. **165:**1720 (Nov. 30) 1957.

[5] International Sanitary Regulations, Foreign Letters, J. A. M. A. **163:**770 (March 2) 1957.

[6] Asia, in Gear, H. S.: Disease Control and International Travel: Review of International Sanitary Regulations, Chron. World Health Organ. **10:**299 (Sept.-Oct.) 1956.

[7] Smallpox and Cholera, Foreign Letters, J. A. M. A. **167:**1768 (Aug. 2) 1958.

COUNCIL ON MEDICAL SERVICE

HOW OLD IS TOO OLD TO WORK?

Interesting clues, with specific application to retirement, as to the answer to the question, "How old is too old to work?" have been reported by S. L. Pressey, professor of psychology at Ohio State University, under the title of "Jobs at 80."[1] Although this study pertained more to persons now living, some surprising examples of performance during the latter decades of life were taken from eras when the average life expectancy was far below the approximately 70 years prevailing today. The studies of Lehman[2] are cited in the following examples: Gladstone was prime minister at 84; a number of our Supreme Court justices served well into their eighth decades (Holmes was 90 when he retired); Tennyson was 80 when he wrote "Crossing the Bar"; Belline at 83 painted one of his masterpieces; Robert Bridges and Thomas Hardy at 85 published poetry that has been long remembered; Verdi was composing at 85; Alexander Humboldt at 89 published his "Cosmology"; and Wundt completed his reminiscences at the age of 88.

Lehman lists 94 persons who continued to produce well into their later decades, 29 of whom produced works of importance at the ages of 80 or over. Pressey points out that, while Lehman's data clearly indicate that the best creative work in the arts and science is usually accomplished quite early in life, his research gives abundant evidence that the creative mind may continue to be productive well into the later years of the life span.

Of more current interest—how about those living and working today into their eighth decades, and further, those engaged in more ordinary areas of activities.[2] Pressey, instead of employing a systematic sampling procedure, merely made an effort to find out if there were such cases of octogenarians, and, if so, of what types. Three sources were explored for case material.[3] 1. Extensive case records of 230 superior older persons in a midwest city. Result: 35 were 80 years of age or over and, of these, 19 were at least occasionally doing some remunerative work. 2. Reports from a total of over 1,000 university students concerned with such problems; these students were requested to report their knowledge of well-known older persons who had done paid work. Result: A total of 127 persons were reported, all of whom were 80 years of age or over and, of these, 9 were 90 or over. 3. A collection of clippings regarding older persons; only those clippings were used which seemed essentially valid. Result: 167 persons past the age of 80 were reported as doing some work.

The three sources which were utilized produced 313 persons aged 80 or over (23 were 90) who were still earning money—who were gainfully employed. Most of the nonagenarians were working either part time or occasionally and included two clergymen, three physicians, three lawyers, one 94-year-old woman who was a receptionist, one man who was justice of the peace, another who operated a cigar stand part time, and one who trained dogs for driving livestock. However, a few were still employed full time; two were bank presidents in small towns; one was a bank teller; and a woman aged 90 was continuing her insurance business.

Among others, all over 80 years of age, but not necessarily 90, were three persons who wrote columns for their local papers, a wood carver who was retouching and restoring paintings and church frescoes, a chemist who was consultant for an industrial organization, a biologist who was consultant for a research institute, and another who published a history of his specialty.

Professional people constituted the largest group (18 physicians and 12 lawyers) but there were 24 skilled artisans, 8 farmers, 8 owners of small stores, 3 clerks, 2 barbers, and several handy men.

Pressey points out that, in view of the informal method of the survey, the figures mean nothing except to show that in all work categories some persons continue useful work into the eighth and ninth decades.

To the above figures probably should be added an undetermined number of persons who had the capacity to work but lacked either the desire or the necessity, and those who had these characteristics but for whom no work was available.

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1. Pressey, S. L.: Jobs at 80, Geriatrics **13**:678-681 (Oct.) 1958.

2. Lehman, H. C.: Age and Achievement, Princeton, N. J., Princeton University Press, 1953.

3. Pressey, S. L.: Potentials of Age: Exploratory Field Study, Genetic Psych. Monograms **56**:159-205 (Aug.) 1957.

MEDICAL NEWS

CALIFORNIA

Heart Symposium in Los Angeles.—Twenty local investigators will present papers on cardiovascular diseases at the third annual Midwinter Symposium of the Los Angeles County Heart Association at the Statler Hotel Jan. 14. The symposium is free to all physicians. Dr. John L. Denney is chairman of the all-day session, which will begin at 9 a. m. and will feature studies in basic sciences, clinical research, and heart surgery. The annual Oliver P. Douglas Memorial prize essay award and honorable mention award will be presented at a luncheon meeting by Dr. Edward Shapiro, past-president of the association.

COLORADO

Combined Meeting in Colorado Springs.—The American College of Physicians, Colorado Region, and the Colorado Society of Internal Medicine will hold a combined meeting at the Broadmoor Hotel, Colorado Springs, Jan. 16-17. Guest speakers include Dr. Philip S. Hench, Rochester, Minn., regent of the college and Dr. H. Marvin Pollard, Ann Arbor, Mich., governor of the college for Michigan. Dr. C. F. Kemper is governor of the college for Colorado, and Dr. William A. H. Rettberg is President of the Colorado Society of Internal Medicine. Three panel discussions are planned with the following moderators:

The Prevention and Management of Hepatitis, Dr. Fred Kern Jr., Denver.
Recent Developments in Rheumatic Diseases, Dr. Charley J. Smyth, Denver.
Anxiety in Clinical Medicine, Dr. Franklin G. Ebaugh, Denver.

For information write Mr. E. R. Loveland, 4200 Pine St., Philadelphia 4.

FLORIDA

Dr. Eyster Honored.—Dr. John A. E. Eyster, of Fort Meyers, emeritus professor of physiology who retired from the University of Wisconsin Medical School, Madison, in 1952, has been honored for "incisive, productive, and humane experimental science" by the Medical Research Association of California which awarded Dr. Eyster its Senior Scientist Award for 1958. In reviewing his research career, the association cited Dr. Eyster for "inspired graduate and medical teaching, and for devotion to the advancement of medicine through animal research."

ILLINOIS

Chicago

Dr. Hesseltine Named Ryerson Professor.—Dr. Henry C. Hesseltine, professor and secretary, department of obstetrics and gynecology, University of Chicago, has been named Mary Campau Ryerson Professor of Obstetrics and Gynecology. Mary Campau Ryerson was the mother of the late Martin A. Ryerson, member of the Board of Trustees of the University from 1890 to 1931 and president from 1892 to 1922 who died in 1932 and who established the Mary Campau Ryerson professorship Dec. 11, 1930, as a tribute to his mother. Dr. Hesseltine became an instructor in obstetrics and gynecology at the University of Chicago in 1931, assistant professor in 1934, associate professor in 1942, secretary of the department and professor in 1949. His appointment to the named chair became effective Nov. 11. He is president of the Chicago Gynecological Society and a diplomate of the American Board of Obstetrics and Gynecology.

LOUISIANA

Graduate Medical Assembly.—The 22nd annual meeting of The New Orleans Graduate Medical Assembly will be held March 2-5, with headquarters at the Roosevelt Hotel. Eighteen guest speakers will participate, and presentations are planned to be of interest to specialists and general practitioners. The program will include 54 discussions in addition to clinicopathologic conferences, symposiums, medical motion pictures, round-table luncheons, and technical exhibits. Following the meeting, arrangements have been made for a clinical tour to Mexico City, Cuernavaca, Taxco, Acapulco, and San Jose Purua, leaving New Orleans March 6 and returning March 21. Information is available at the office of the Assembly, Room 103, 1430 Tulane Ave., New Orleans 12.

MARYLAND

Dr. Lillie Receives Award.—The first Sustaining Membership award of the Association of Military Surgeons of the United States was given to Dr. Ralph D. Lillie, chief of laboratory and histochemistry, National Institute of Arthritis and Metabolic Diseases, National Institutes of Health, Bethesda, "for his accomplishments in the field of histochem-

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Physicians are invited to send to this department items of news of general interest, for example, those relating to society activities, new hospitals, education, and public health. Programs should be received at least three weeks before the date of meeting.

istry" at the recent meeting of the association. This award, consisting of a scroll and an honorarium of $500, is given by the Sustaining Membership Group of the association to government employees who have distinguished themselves by "outstanding work in the field of research."

MASSACHUSETTS

Lectures on Medicine and Law.—The Right Honorable Lord Nathan, P. C., of England, spoke on "Medical Negligence and the Law" at Boston University School of Medicine, Nov. 18. Lord Nathan was the first speaker in a series of lectures sponsored by the Boston University Law-Medicine Research Institute. Director of the Institute is Prof. William J. Curran of Waban, Mass. Lord Nathan is a member of the International Law Association, Medico-Legal Society, and the British Section, International Commission of Jurists (Member of Council). Future speakers in the series sponsored by the institute will talk on Law and Behavioral Science; Heart Disease and Stress; Demonstrative Medical Evidence; Medicine, Morals and The Law; and Accidents and Accident Repeaters.

MICHIGAN

Establish Gordon B. Myers Award.—The Gordon B. Myers award in internal medicine has been established at Wayne State University College of Medicine, Detroit, "in recognition of Dr. Myers' inspiring leadership as chairman of the department of medicine for over 20 years." The award has been made possible by contributions from former residents and fellows who received postgraduate training under Dr. Myers. An award of $100 and a scroll is to be made annually to the graduating senior who has distinguished himself above all others in his class in courses given by the department of medicine. The recipient of the award will be chosen by the chairman and the full-time faculty of the department. Dr. Myers resigned as chairman of the department of medicine in 1958. As professor of medicine, he heads the university service in internal medicine at Harper Hospital.

MINNESOTA

Guest Lecture.—Mr. R. Milnes Walker, professor of surgery in the University of Bristol, Bristol, England, gave a lecture on "Some Problems of Portal Hypertension" at the Mayo Clinic and Mayo Foundation, Rochester, Nov. 7.

NEW JERSEY

Typhoid Fever.—The National Office of Vital Statistics has revealed that Dr. Hugh D. Palmer, New Jersey district state health officer, reported an outbreak of six cases of typhoid fever in a community of about 1,000 population. On Oct. 24 a 42-year-old woman died with a tentative diagnosis of typhoid fever. This diagnosis was subsequently confirmed. By Nov. 8 other cases had developed in five persons ranging in age from 2 to 16 years. The diagnoses were confirmed by isolation of *Salmonella typhi* from stool specimens and/or agglutination titers. Blood specimens were positive for "O" and "H" antigens. The community is without public water and sewerage facilities. The houses in which the illnesses occurred have cesspools and shallow wells.

NEW YORK

Dr. Hodge Named Department Chairman.—Appointed as professor of pharmacology and chairman of the new department of pharmacology, University of Rochester School of Medicine and Dentistry, is Harold C. Hodge, Ph.D., who has been a professor of pharmacology and toxicology at the Atomic Energy Project of the medical center since 1946.

Society News.—The Medical Society of the State of New York, 750 Third Ave., New York 17, has announced the appointment of Dr. Herbert T. Wagner as executive director.——The officers of the New York Allergy Society for 1958-1959 are as follows: president, Dr. Aaron D. Spielman, New York City; president-elect, Dr. S. Senior Sack, Flushing; vice-president, Dr. Russell C. Grove, New York City; secretary, Dr. Sheppard Siegal, New York City; treasurer, Dr. Joseph H. Fries, Brooklyn; and assistant secretary-treasurer, Dr. Murray Dworetzky, New York City.

New York City

Memorial Fellowship in Dermatology.—Phi Delta Epsilon Fraternity's Charles R. Rein Memorial Fund has awarded a fellowship in dermatology to New York University. It honors the late Dr. Charles R. Rein of the department of dermatology and syphilology of the NYU Post-Graduate Medical School and is to go annually to the candidate selected by Dean Donal Sheehan and the chairman of the department of dermatology and syphilology. Dr. Laszlo Biro, a resident in the dermatologic service at The Bellevue Hospital Center, has been selected to be the first recipient of the fellowship. He will engage in research on the serology, immunology, and epidemiology of treponemal and staphylococcal diseases and other infections. The three-year fellowship, made possible through the contributions of fraternity members and friends to a memorial fund, was established in May, 1957, on the death of Dr. Rein, a past-grand consul of the fraternity.

Personal.—Dr. H. Houston Merritt, acting dean of the Faculty of Medicine and acting vice-president in charge of medical affairs at Columbia University College of Physicians and Surgeons, has been elected a vice-president of United Cerebral Palsy Associations Inc., at the organization's ninth annual conference.——Dr. Abraham M. Rabiner has been named professor emeritus of neurology at the State University of New York Downstate Medical Center in Brooklyn. A member of the center's faculty since 1937 when it was still the Long Island College of Medicine, Dr. Rabiner retired as professor and head of the division of neurology on Aug. 31. On the same date he retired as director of neurology at the Kings County Hospital.——Dr. Frederick S. Reiss, associate clinical professor of dermatology, New York University, Postgraduate Medical School, has been elected honorary member of the Sociedade Portuguesa de Dermatologia e Venereologia.

NORTH CAROLINA

Program to Aid Child Amputees.—The Duke University Medical Center's Orthopedic-Amputee Clinic has been selected to participate in a national program aimed at helping child amputees. Sponsored by the Prosthetic Research Board of New York University under the National Research Council, the program will help parallel for children the progress made in artificial limbs for veterans since World War II. Also, the program will promote the expansion of child amputee clinics throughout the United States. The Duke amputee clinic, headed by Dr. J. Leonard Goldner, professor of orthopedic surgery, is one of nine chosen to take part in the program. Beginning Jan. 1, the Duke clinic will collect special data on the problems and progress of all amputee patients under 16 years of age. This and similar information gathered at other amputee clinics over the nation will be brought together during periodic meetings of clinic heads. Other amputee clinics participating with Duke in the new program are located in Atlanta, Ga.; Birmingham, Ala.; Philadelphia; Grand Rapids, Mich.; Buffalo, N. Y.; Los Angeles; Chicago; and New York City. The Duke clinic, established in 1955, uses a team approach to the problems of amputees. Team members include an orthopedic surgeon, a prosthetist (artificial limb maker), a physical therapist, an occupational therapist, and a social service worker.

OHIO

Dr. Beck Gives Kuntz Lecture.—Dr. Claude S. Beck, professor of cardiovascular surgery, Western Reserve University School of Medicine, Cleveland, delivered the annual Albert Kuntz lecture Dec. 15 on "Coronary Heart Disease Blood Supply to Ischemic Muscle." The lecture is sponsored by the Phi Chi Medical Fraternity of the Saint Louis University School of Medicine.

Physicians Meeting in Cincinnati.—The Ohio Regional meeting of the American College of Physicians will be held at the Netherland Hilton Hotel, Cincinnati, Jan. 22, with Dr. A. Carlton Ernstene, governor of the college for Ohio, opening the program. Dr. Dwight L. Wilbur, president of the college, will be the principal speaker at the banquet at 7 p. m. A two-part clinical pathological conference will be conducted in the afternoon. A panel discussion on "Status of the Internist in Medical Care Plans" will be moderated by Dr. George J. Hamwi, Columbus. Sixteen papers will be read by title. For information write Dr. Eugene H. Sterne Jr., Veterans Administration Hospital, 3200 Vine St., Cincinnati 20.

OREGON

Plan Student Activities Building.—A new $350,000 Student Activities Building for the University of Oregon Medical-Dental School campus in Portland is being planned. At the late October meeting of the Oregon State Board of Higher Education, preliminary plans were approved and permission was given to finalize the blueprints for the two-story building. To be located in the canyon west of the Medical School Hospital and south of the Medical Science and Administration buildings, the 100- by 116-foot structure will be constructed of reinforced concrete and will include athletic and recreational facilities. A regulation size basketball court with seating areas will take up most of the second floor. Coordinating the planning of the facility has been W. A. Zimmerman, Medical and Dental School business manager. The building will be financed through student building fees which have been accumulating since 1945. About half the money needed is now available, and the rest will be made up through bonding of future building fee income.

PENNSYLVANIA

Meeting of Physicians in Philadelphia.—The American College of Physicians will hold its 20th annual reunion of Eastern Pennsylvanians at the Sheraton Hotel, Philadelphia, Jan. 23. The program is designed to encourage participation of physicians from all parts of Eastern Pennsylvania, and a cordial invitation is extended to physicians from Delaware and New Jersey. Dr. William A. Jeffers is governor of the college for Eastern Pennsylvania. Nineteen papers are scheduled for presentation at the three sessions. At the banquet at 7 p. m. with Dr. Allen W. Cowley Sr., Harrisburg, as toastmaster, Dr. Dwight L. Wilbur, San Francisco, president of the college, will give the address of the evening on "The Third Person in Medicine." For information write Mr. E. R. Loveland, Executive Secretary, American College of Physicians, 4200 Pine St., Philadelphia 4.

Philadelphia

Dr. Gyorgy Honored.—The University of Heidelberg has conferred the degree of honorary medical doctor on an alumnus and former faculty member, Dr. Paul Gyorgy, professor of pediatrics at the University of Pennsylvania, and chief of the pediatric service of the Philadelphia General Hospital. The honor, to Dr. Gyorgy, which was proposed by the faculty of Heidelberg, and approved by the Rector and the University Senate, was presented "in recognition of his many scientific achievements in the past." Also voted an honorary M.D. was Dr. Otto Warburg, of Berlin, a Nobel Laureate and developer of the Warburg Apparatus. Dr. Gyorgy is credited with the discovery of riboflavin.

Personal.—Dr. Henry L. Bockus, chairman, department of internal medicine, University of Pennsylvania Graduate School of Medicine, has been elected to membership on the executive committee of MEDICO, (Medical International Cooperation), a private, nonprofit organization that furnishes American medical personnel, techniques, drugs, and supplies to the newly developing countries of Asia, Africa, and Latin America. A division of the International Rescue Committee, MEDICO sends teams of American physicians and surgeons, and other types of private American medical assistance to areas of the world where they are needed.—— Dr. I. S. Ravdin, John Rhea Barton Professor of Surgery, University of Pennsylvania, has been elected to the chairmanship of the Pennsylvania Plan to Develop Scientists in Medical Research at the recent meeting of the plan's executive committee, succeeding Dr. Norman H. Topping, formerly vice-president of the university who was appointed president of the University of Southern California, Los Angeles, in August.

TENNESSEE

Society Election.—The Memphis Thoracic Society, an organization of Memphis and Mid-South thoracic surgeons, internists, and medical chest physicians, has elected the following officers for 1959: Dr. Francis H. Cole, president, succeeding Dr. Felix A. Hughes Jr.; Dr. John C. King, vice-president; and Dr. Glenn E. Horton, secretary-treasurer (reelected). Physicians in the Mid-South area are invited to attend the meetings. Information may be obtained from the Secretary-Treasurer, Memphis Thoracic Society, 4915 Mockingbird Lane, Memphis 17, Tenn.

Walker Surgical Club Formed.—During the recent meeting of the American College of Surgeons in Chicago a club was formed in honor of Dr. Matthew Walker, chairman, department of surgery, Meharry Medical College, Nashville. The organization, to be known as the "Walker Surgical Club," is composed of surgeons who have received surgery training under Dr. Walker; there are presently 50 members in the club. At the organizational meeting Dr. Walker was presented with a silver tray bearing the inscription, "presented to Dr. Matthew Walker on the occasion of the founding of the Walker Surgical Club in deep appreciation of his unselfish service in the training of surgeons." Dr. Waldo L. Cain, Detroit, was elected chairman of the club and Dr. George W. Hilliard, secretary-treasurer. The club will meet once yearly during the meeting of the American College of Surgeons and has as its purpose the furtherance of the surgical program at Meharry.

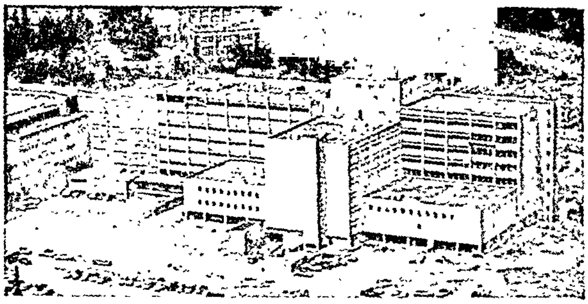
TEXAS

Dr. Waksman to Lecture.—The Alpha Nu Chapter of the Phi Delta Epsilon Fraternity at the University of Texas Medical Branch, Galveston, will hold the Meyer Bodansky Lectureship Jan. 23. The guest speaker will be Selman A. Waksman, Ph.D., director, Rutgers Institute of Microbiology, New Brunswick, N. J.

Texas Society on Aging Formed.—Mr. Herbert Shore, of Dallas, has been chosen as first president of the new Texas Society on Aging, formed recently at the Driskill Hotel in Austin. Dr. Ernest W. Keil, Temple, is president-elect; Hiram J. Friedsam, Ph.D., Denton, is vice-president, and Mrs. William B. Ruggles, of Dallas, will serve as secretary-treasurer. The Texas Society on Aging is the product of a merger between the Texas Geriatric Society and the Texas Gerontological Society and carries as its slogan, "Aging is everybody's business." The new society has a membership of 600 and much of its work is in relation to the Texas Interim Legislative Committee on Aging. The Texas Society on Aging is a chapter of the national Gerontological Society, Inc., and is a nonpolitical, nonprofit, scientific society dedicated to fostering the growth and dissemination of knowledge relating to that process in medicine, physical and mental health and care, economics, employment, recreation, education, social welfare, housing and other fields, in order to advance the well-being of older persons in American culture. The society publishes a newsletter on developments in aging throughout the state and nation.

WASHINGTON

Plan Dedication of Teaching Hospital.—Dedication services for the new University of Washington Teaching Hospital have been set for April 18. Designed for teaching and research, the new hospital will accept referred patients from all parts of the state and will be a training center for 18 health professions. Governor Albert D. Rossellini will be the principal dedication speaker. The hospital, adjacent to the Health Sciences Building at the southern edge of the university campus, has been built in two stages. Unit I, housing offices and laboratories for departments concerned with patient care, was completed in 1954. Unit II, under construction, contains central service and diagnostic facilities, and outpatient clinic, and beds for 300 inpatients. The dedication will be followed by a public open house April 18 and 19.



The new University of Washington Teaching Hospital, Seattle.

GENERAL

Examinations by Board of Nutrition.—The American Board of Nutrition will hold the next examinations for certification as a specialist in human nutrition, during the week of April 12-18, 1959, in Atlantic City, N. J. Candidates who wish to be considered for these examinations should forward applications to the Secretary's Office not later than March 1. Application forms may be obtained from the Secretary, Dr. Robert E. Shank, Department of Preventive Medicine, Washington University School of Medicine, Euclid and Kingshighway, St. Louis.

Organize Institute of Medical Climatology.—On Nov. 20 the American Institute of Medical Climatology, a nonprofit organization, was officially formed in Philadelphia. Members include physicians, scientists, and educators. The institute sponsors a program of continuous research and education into all phases of the relationship between weather and human life. Twelve sections implement the work of the institute: medicine, biology, psychology, air pollution, biostatistics, institutional planning, industrial planning, atmospheric electricity, meteorology, public health, medical hydrology, engineering, and instrumentation. Charter members of the institute have elected the following officers: Dr. George M. Piersol, president; Very Rev. James A. Donnellon, O.S.A., first vice-president; and Harold W. Schaefer, second vice-president. Dr. Igho H. Kornblueh, 1618 Allengrove St., Philadelphia 24, is secretary.

Bahamas Serendipity Conference.—The first Bahamas Serendipity Conference will be held Jan. 18-31 at the British Colonial Hotel, Nassau, Bahamas. The conference "aims at bringing together people from various disciplines, research workers, scientists, and clinicians, to look together at a problem from their respective points of view." The following will participate as "animateurs" to stimulate discussion under the following themes:

Serendipity	R. Keith Cannan, D. Sc., Washington, D. C.
Kidney	Alfred Gilman, Ph.D., New York, N.Y.
Chemical Synthesis	Henry B. Hass, LL.D., New York City.
Discovery	Edward C. Kendall, Ph.D., Princeton, N.J.
Enzymology	Dr. I. Arthur Mirsky, Pittsburgh, Pa.
Scientific Accidents	Bernard Edward Schaar, Chicago, Ill.
Endocrinology	Dr. Abraham G. White, New York, N.Y.

Dr. B. L. Frank is the organizing physician for the Bahamas Conferences. Reservations should be made by writing directly to "Bahamas Conferences," P. O. Box 4037, Fort Lauderdale, Fla.

Report Lower Accident Rate for Large Cities.—A study by the Metropolitan Life Insurance Company's statisticians of accident mortality in the 41 U. S. cities which had 250,000 or more inhabitants at the time of the 1950 census has revealed that accident death rates for residents of these cities averaged 49.2 per 100,000 in 1955-56 as compared with 56.8 for the population of the U. S. as a whole. Of the 41 cities under review, 32 had rates below the national average. In spite of this, it is pointed out, residents of the large cities suffer a heavy loss of life from accidents, each year about 18,000 of them being fatally injured in mishaps of one kind or other. The accident death rate in 1955-56 in the large cities ranged from a low of 37.8 per 100,000 for Jersey City to a high of 77. for Indianapolis. The five cities with one million or more inhabitants in 1950—New York, Chicago, Los Angeles, Philadelphia, and Detroit—as a group experienced a lower rate than did groups composed of the cities with populations in various ranges under one million. For the 41 cities as a group, the motor vehicle accident death rate was about 31% below the national average.

Listing of Government Scientific Information.—The National Science Foundation has published the first bulletin in a new series which, when completed, will represent an inventory listing of all significant scientific information sources or activities within the federal government. Reportedly, the series should prove of value as an aid in directing scientists, engineers, and research librarians to the appropriate sources of government-sponsored or -supported research information in specific scientific fields. The preparation and publication of this series is one of the tasks undertaken by the foundation's Science Information Service under its Unpublished Research Information (URI) program. The primary objective of this program is to make unclassified unpublished scientific research information easily accessible and readily available to all U. S. scientists and engineers, in and out of government. Comments or suggestions concerning the intended purpose of this series, as well as the contents of specific issues, should be addressed to: National Science Foundation, Science Information Service, Washington 25, D. C., Attention: URI Program Director.

Awards in Anesthesiology.—The first Mead Johnson awards for graduate training in anesthesiology have been granted to three physicians. Dr. Ralph S. Sappenfield, of Miami, Fla., president of the American Society of Anesthesiologists, has announced that the society would award the scholarships annually. The scholarships are made possible by funds granted by Mead Johnson & Company, Evansville, Ind. Recipients of the first awards are: (1) Dr. Robert Douglas Winship, Berkeley, Calif., a resident physician at the University of California Hospitals, San Francisco; (2) Dr. Jack Allan Gray, Dallas, Texas, who has been a resident physician in anesthesiology at Parkland Memorial Hospital since July, 1957; and (3) Dr. Thomas Franklin Wooden, who will become a resident physician in anesthesiology at Indiana University Medical Center, Indianapolis, following completion of Army service. The Mead Johnson awards are made to physicians engaged in residency training for specialization in anesthesiology, and are granted to "deserving physicians on the basis of meritorious work in clinical and research fields, and general qualifications for success in the specialty." Selection of physicians is carried out in behalf of the society by trustees of the Anesthesia Memorial Foundation, headed by Dr. John S. Lundy, of Rochester, Minn.

Society News.—New officers of the **Southwestern Dermatological Society** elected at Tucson are: Dr. Earle R. Pace, Santa Fe, president; Dr. George A. Waldriff, Albuquerque, vice-president; Dr. Henry D. Garrett, El Paso, secretary-treasurer.——Dr. Leona Baumgartner, New York City, became president of the **American Public Health Association** at the conclusion of its 86th annual meeting in St. Louis Oct. 27-31. Dr. Malcolm H. Merrill, Berkeley, was named president-elect, and will become president at the 87th annual meeting in Atlantic City Oct. 19-23, 1959. Vice-presidents elected were Drs. Abraham Horwitz, Santiago, Chile; Frederick B. Roth, Regina, Saskatchewan, Canada; and Estella Ford Warner, Albuquerque, N. M. Executive director is Dr. Berwyn F. Mattison, with headquarters at 1790 Broadway, New York 19.——New officers of the **American Society of Anesthesiologists** are as follows: president, Dr. Daniel C. Moore, Seattle, succeeding Dr. Ralph S. Sappenfield, Miami, Fla.; president-elect, Dr. Leo V. Hand, Boston; first vice-president, Dr. William O. McQuiston, Peoria, Ill.; second vice-president, Dr. George J. Thomas, Pittsburgh; secretary, Dr. Joseph E. Remlinger Jr., Chicago; assistant secretary, Dr. Robert L. Patterson, Pittsburgh; treasurer, Dr. Albert M. Betcher, New York City; assistant treasurer, Dr. Edwin Emma, Flushing, N. Y.

Awards to Medical Students.—The five winners in each of three divisions of the 1958, 13th annual Schering Award Competition have been announced by Dr. Richard McCormick, chairman of the award committee. Fifteen winners shared in the $5,700 prize money established by Schering Corporation, with individual prizes ranging from $1,000 for first prize, to $50 for fifth prize. Marvin Gottlieb, of the University of Tennessee College of Medicine, Memphis, who has won two similar awards in 1956 and 1957, received $1,000 for his paper on "The Mechanism and Current Concepts on the Treatment of Nausea and Vomiting." Frank A. Oski, of the University of Pennsylvania School of Medicine, Philadelphia, also received a first prize of $1,000 for his paper, "Current Trends in Corticosteroid Therapy in Pediatrics." The third first-place winner was Mrs. Helen S. Kaplan, of the New York Medical College, New York City, who received $1,000 for her paper on "Use of Tranquilizer Therapy in Office Practice." The three second-place winners receiving $500 each for their prize winning papers are: Marvin Anderson Jr., University of Michigan Medical School, Ann Arbor; Martha Bouck, of Queen's University Faculty of Medicine, Kingston; and Larry Samuels, University of Illinois College of Medicine, Chicago. Third, fourth, and fifth place prizes were of $250, $100, and $50, respectively. The Schering award, which began in 1940, seeks to encourage among the nation's medical students original reporting and exploration of recent developments in therapy.

Scientific Exhibit Assembly.—Medical students, interns, and residents are being urged to participate in the second annual national scientific exhibit assembly of the Student American Medical Association to be held in Chicago April 30-May 2. The program was inaugurated in 1958 and is dedicated to the contributions of medical students to research and to the advancement of the scientific exhibit as a primary medium of communication in the profession. Arrangements have been made for space to hold a total of 40 scientific exhibits; of these, 20 will be by students and 20 by interns and residents. The SAMA-Lakeside Laboratories awards will again be given, with the special honor of free all-expense trips to the American Medical Association convention and the privilege of exhibiting in the AMA's scientific assembly, for the top student and the top intern or resident. Cash prizes and plaques will be given, with $500, $250, and $100 for award-winning exhibits by students, and equal awards for those by interns and residents. Lakeside Laboratories supports the awards and the trips. Applications must be obtained from SAMA (address Mr. Russell Staudacher, Executive Secretary, Student American Medical Association, 430 N. Michigan Ave., Chicago 11) and returned no later than Feb. 1, 1959. On Feb. 14, the 40 chosen exhibitors will be announced. These must complete their exhibits and ship them to Chicago at their own expense. Space and basic materials such as backdrop, table, chairs and lighting, will be provided free by SAMA.

Program for Health Scholarships.—The National Foundation, to help overcome shortages of personnel in the health field, has announced a multimillion-dollar scholarship program, a first step in its new expanded program. The present scholarship and fellowship program will be continued but modified and expanded where necessary. This program over the years has added over 7,600 especially trained people to those prepared to work in research and patient care. Mr. Basil O'Connor, president of the foundation, summarized the new program as follows:

> The National Foundation will offer annual health scholarships to help provide four years of College education in medicine, medical social work, nursing, physical therapy, and occupational thearpy.
>
> A minimum of 505 Health Scholarships will be offered each year, the first of them before the end of the 1959 school year. They will be made available on a geographic basis with heavily populated states receiving as many as 25—or five for each of the five professions—and with no state or territory receiving less than five health scholarships, a minimum of one for each of the five professions.
>
> The foundation's chapters, numbering more than 3,100 will seek and accept scholarship applications, pass them on to state or territorial professional committees for selection, and will present awards to winners.
>
> Health scholarships will be available to student citizens of the U. S. in the 49 states, the District of Columbia, Hawaii, and Puerto Rico.
>
> Over the next 10 years this program will cost at least $12,000,000. Each scholarship awardee will receive $500 a year for four years, or a total of $2,000, providing that scholastic standards are maintained. The 505 health scholarships each year will cost over one million dollars.

Because education requirements of the five professions vary, scholarships will be made available in nursing, physical therapy and occupational therapy to graduating high school students; in medical social work, at the college junior year, extending through two years of required graduate work; and in medicine, at the college junior, senior, or first graduate year, depending upon the requirements of the medical school. For information write the National Foundation, 800 Second Ave., New York 17, N. Y.

Tuberculosis Among Kindergarten Children.—A community-wide study of the tuberculin tes among kindergarten children, conducted in Kansa City, Mo., with the aid of a Christmas Seal gran from the National Tuberculosis Association and it medical section, the American Trudeau Society, ha revealed a relationship between the size of the tes and the presence of active tuberculosis amon adults in contact with the children; it also reveale that there was no decrease in tuberculosis infectio rates among kindergarten children in the 10-yea period of the study, despite a marked decline i tuberculosis mortality in the community. In th survey the histoplasmin test for histoplasmosis infection was given as well as the skin test for tube culous infection. During the period covered, fro 1947 to 1957, the tests were given 35,995 kinde garten children. For seven years, nonreactors t tuberculin were retested in the first grade and was found that, on the average, 1% of the whit children and 1.4% of the Negroes had converted t positive. The rate of conversion did not fall durin the period covered. The study showed that a number of new previously unknown cases of tuberc losis was found in a follow-up of the adult contact The percentage of children who became infecte during the first year in school was relatively hig and showed no tendency to decline over the perio of seven years' observation. This was despite th fact that the death rate from tuberculosis for Kansas City fell during the 10 years of the survey fro 31.3 to 11.7. On original testing in kindergarte there were 597 reactors to tuberculin among th 35,995 children, the percentage being higher amon the Negro children than among the white childre conversely, the percentage of reactors to histopla min in this city where histoplasmosis is endem was higher among the white children. The Hea of America Tuberculosis Association, Kansas Cit Mo.; the University of Kansas School of Medicin Kansas City, Kan.; the Kansas City, Mo., Board Education; and the Communicable Disease Cente U. S. Department of Health, Education, and We fare, Atlanta, Ga., cooperated in the study.

Levels of Radioactivity in Milk.—The U. S. Publi Health Service has reported that radioactivity levels in milk collected during August from 10 sampling stations across the country continued to b below the current permissible levels recommende by the National Committee on Radiation Protectio and Measurements. Radiation levels from six stations showed a decline in strontium-90 compare with July data. These were the stations in th milksheds serving Austin, Texas; Cincinnati; Fargo N. D.; New York City; Salt Lake City; and St Louis. Three stations, in the milksheds serving Atlanta, Ga., Chicago, and Sacramento, Calif., reported slight increases over July. A tenth station, in the milkshed serving Spokane, Wash., was added to the network in August. Levels of four other specific radioactive elements in milk—iodine-131, strontium-89, barium-140, and cesium-137—were also found to vary not only between samples collected from different stations of the network, but, also, between samples taken from the same stations. From past experience, month-to-month fluctuations in levels reportedly are to be expected. The National Committee on Radiation Protection and Measurements is a scientific group established under the sponsorship of the National Bureau of Standards with the cooperation of radiological organizations in the United States. The permissible levels recommended by the committee refer to average exposure over an entire lifetime and may be exceeded for short periods of time. The levels are subject to periodic evaluation and revision as new scientific data become available. Monthly composite samples of milk obtained through the cooperation of state and municipal health agencies, state departments of agriculture, and the dairy industry are analyzed for specific radioactive elements at the Robert A. Taft Sanitary Engineering Center operated by the Public Health Service in Cincinnati. About six weeks are required to complete the laboratory analysis of the samples. Average exposure over an extended period of time reportedly is the significant factor in interpreting the public health effects. Data are reported in terms of micromicrocuries per liter. For the period ending August, 1958, the 12-month average levels for these elements were: strontium-90 ranged from 4.2 to 10.7; iodine-131, from 29 to 220; strontium-89, from 24 to 115; barium-140, from 17 to 95; cesium-137, from 53 to 73.

FOREIGN

Award in Laryngology.—The International Committee for the Gould Award has announced that the selection of the recipient for the year 1958 is Prof. Fumio Nakamura, M.D., Kyoto Prefectural Medical College, Kyoto, Japan, for his electrophysiologic studies of laryngeal function. The Gould award is presented annually for "outstanding research in laryngology" to encourage and reward fundamental investigations in this field. The international committee for 1959 will consist of Sir Victor Negus, 149 Harley St., London, W.1; Prof. Cotoji Satta, No. 111 Morikawa-cho, Bunkyo-ku, Tokyo; and Dr. Hans von Leden, Medical Director, The William and Harriet Gould Foundation, 30 N. Michigan Ave., Chicago 2. The amount of the award has been increased to $300.

Medical School and Teaching Hospital in Belgian Congo.—Founded three years ago under the sponsorship of the University of Louvain, one of the oldest schools in Europe, Lovanium University in Leopoldville, the Belgian Congo, is making progress toward the organization of a complete university curriculum. To assist in the development of the medical school and the university hospital, The Rockefeller Foundation has appropriated 10,952,500 Belgian Congo francs (about $230,000) for use during the next three years. When the medical school opened in 1954, five students were enrolled; this number has now risen to 37, of whom 15 are in the first year of the course. The formative years of the school have been devoted primarily to the basic sciences and morphological studies. By the time the students reach the clinical stage of their training, the new university hospital is expected to be ready for use. The university obtained the hospital at 20% of its actual cost through an agreement to operate it for the medical needs of the region for which the government is responsible. When completed, the hospital will have a capacity of 1,000 beds and represent an investment of 4 million dollars. Two wings are in operation. The university has undertaken responsibility for public health activities in two nearby native villages, Ndjili and Matete, with a combined population of 14,000. University students, who will participate in the medical and health services, will have direct practical experience with community problems as well as with in-patients in the university hospital. The new university is coeducational and permits no racial, religious, or political discrimination. At present the university consists of a Faculty of Science which is preparing students for studies in medicine and agriculture; the Faculty of Medicine; a Faculty of Administration and Social Science which is to become a College of Law; and a Faculty of Education which is now preparing teachers for the secondary schools of the Congo and which will later be developed into a College of Liberal Arts. The Government of the Congo, the Mining Union, and private sources are all contributing to the construction of university buildings.

CORRECTIONS

Treatment of Metastatic Thyroid Carcinoma.—In the Question and Answer concerning metastatic thyroid carcinoma (THE JOURNAL, Dec. 6, 1958, page 1953) in the 10th line of the answer the symbol "μc" for microcurie was given instead of mc. for millicurie.

Journal "Backbones" December 27.—Some 20,000 copies of THE JOURNAL of Dec. 27, 1958, had been mailed before it was discovered that the wrong date (Dec. 17) had been printed on the "backbone" of those copies. The date on the front cover and inside the Dec. 27 issue is correct. We regret that this error occurred.

EXAMINATIONS AND LICENSURE

NATIONAL BOARD OF MEDICAL EXAMINERS

National Board of Medical Examiners: Part II only, April 21-22; Parts I and II, June 16-17; Part I only, Sept. 9-10. Examinations must be received at least six weeks in advance of a specific examination date. Examining centers established after close of registration. Exec. Sec., Dr. John P. Hubbard, 133 South 36th St., Philadelphia 4.

EDUCATIONAL COUNCIL FOR FOREIGN MEDICAL GRADUATES, INC.

Educational Council for Foreign Medical Graduates, Inc.: Stations around the world, Feb. 17. Deadline for foreign applications was Nov. 17. The following examination will be held Sept. 22 with application deadline of June 22. Exec. Director, Dr. Dean F. Smiley, 1710 Orrington Ave., Evanston, Ill.

BOARDS OF MEDICAL EXAMINERS

Alabama: *Written.* Montgomery, June 16-18. Sec., Dr. D. G. Gill, State Office Bldg., Montgomery 4.

Alaska:* On application in Anchorage and Juneau. Sec., Dr. W. M. Whitehead, 172 South Franklin St., Juneau.

Arizona:* *Written Examination and Reciprocity.* Phoenix, Jan. 14-16. Sec., Dr. Thomas H. Bate, 2910 North 7th Ave., Phoenix.

Arkansas:* *Examination and Reciprocity.* Little Rock, June 11-12. Sec., Dr. Joe Verser, Harrisburg.

Connecticut:* *Regular. Examination.* Hartford, March 10-12. Acting Sec., Dr. Louis P. Hastings, 160 St. Ronan St., New Haven. *Homeopathic. Examination.* Derby, Jan. 13. Sec., Dr. Donald A. Davis, 38 Elizabeth St., Derby.

Delaware: *Written Examination and Endorsement.* Dover, Jan. 13-15, Jan. 22. Sec., Dr. Joseph S. McDaniel, Professional Bldg., Dover.

Florida:* *Examination.* Miami Beach, June 22-24. Sec., Dr. Homer L. Pearson, 901 N.W. 17th St., Miami 36.

Georgia: *Examination and Reciprocity.* Atlanta, June. Sec., Mr. C. L. Clifton, 224 State Capitol, Atlanta 3.

Guam: *Subject to Call.* Act. Sec., Dr. F. L. Conklin, Agana.

Hawaii: *Examination.* Honolulu, Jan. 12-13. Sec., Dr. I. L. Tilden, 1020 Kapiolani St., Honolulu.

Idaho: *Examination and Endorsement.* Boise, Jan. 12-14. Sec., Mr. Armand L. Bird, 364 Sonna Bldg., Boise.

Illinois: *Examination and Reciprocity.* Chicago, Jan. 26-30. Supt. of Registration, Mr. Fredric B. Selcke, Capitol Bldg., Springfield.

Kansas:* *Examination.* Kansas City, Jan. 16-17. *Reciprocity.* Kansas City, Jan. 14. Sec., Dr. F. J. Nash, 364 New Brotherhood Bldg., Kansas City.

Maine: *Examination.* Portland, March 10-12. *Endorsement.* Portland, March 10. Sec., Dr. Adam P. Leighton, 142 High St., Portland.

Massachusetts: *Examination.* Boston, Jan. 13-16. Sec., Dr. Robert C. Cochrane, State House, Room 37, Boston 33.

Michigan:* *Examination.* Ann Arbor and Detroit, June 8-10. Sec., Dr. E. C. Swanson, 118 Stevens T. Mason Bldg., West Michigan Ave., Lansing 8.

Minnesota:* *Examination.* Minneapolis, Jan. 20-22. *Reciprocity.* St. Paul, February. Sec., Dr. F. H. Magney, 230 Lowry Medical Arts Bldg., St. Paul.

Montana: *Examination and Reciprocity.* Helena, April 7. Sec., Dr. Thomas L. Hawkins, 555 Fuller Ave., Helena.

Nebraska:* *Examination.* Omaha, June. Director, Mr. Husted K. Watson, Room 1009, State Capitol Bldg., Lincoln 9.

New Hampshire: *Examination and Endorsement.* Concord, Mar. 11-14. Sec., Dr. Edw. W. Colby, 61 So. State St., Concord.

New Jersey: *Examination.* Trenton, Jan. 20-23. Sec., Dr. Royal A. Schaaf, 28 W. State St., Trenton.

New Mexico:* *Examination and Reciprocity.* Sante Fe, May 18-19. Sec., Dr. R. C. Derbyshire, 227 East Palace Ave., Santa Fe.

North Carolina: *Reciprocity.* Southern Pines, Jan. 17. *Examination.* June. Asst. Sec., Mrs. Louise J. McNeill, 716 Professional Bldg., Raleigh.

North Dakota: *Examination and Reciprocity.* Grand Forks, Jan. 7-10. Sec., Dr. C. J. Glaspel, Grafton.

Oklahoma:* *Examination.* Oklahoma City, June 2-3. Exec. Sec., Mrs. E. L. Haidek, 813 Braniff Bldg., Oklahoma City.

Puerto Rico: *Examination and Reciprocity.* San Juan, March 3. Acting Secretary, Dr. Herminio Mendez Herrera, Box 9156, Santurce.

South Dakota:* *Examination.* Sioux Falls, Jan. 20-21. Exec. Sec., Mr. John C. Foster, 300 First National Bank Bldg., Sioux Falls.

Utah: *Examination.* Salt Lake City, July 8-10. Dir., Mr. Frank E. Lees, 324 State Capitol Bldg., Salt Lake City 1.

Washington:* *Examination.* Seattle, Jan. 12-14. Sec., Mr. Thomas A. Carter, Capitol Bldg., Olympia.

Wisconsin:* *Examination and Reciprocity.* Madison, Jan. 13-15. Sec., Dr. Thomas W. Tormey, Jr., 1140 State Office Bldg., 1 West Wilson St., Madison.

Wyoming: *Examination and Reciprocity.* Cheyenne, Feb. 2. Sec., Dr. Franklin D. Yoder, State Office Bldg., Cheyenne.

BOARDS OF EXAMINERS IN THE BASIC SCIENCES

Arkansas: *Examination.* Little Rock, May 4-5. Sec., Dr. S. C. Dellinger, University of Arkansas, Fayetteville.

Connecticut: *Examination.* New Haven, Feb. 14. Exec. Asst., Mrs. Regina G. Brown, 258 Bradley St., New Haven 10.

Florida: *Examination.* Miami, June 6. Sec., Mr. M. W. Emmel, University of Florida, Box 340, Gainesville.

Iowa: *Examination.* Des Moines, Jan. 13. Sec., Dr. Elmer W. Hertel, Wartburg College, Waverly.

Kansas: *Examination.* Kansas City, June. Sec., Dr. L. C. Heckert, Pittsburg.

Michigan: *Examination.* Ann Arbor and Detroit, Feb. 12-13. Sec., Mrs. Anne Baker, 116 Stevens T. Mason Bldg., West Michigan Ave., Lansing.

New Mexico: *Examination.* Santa Fe, Jan. 18. Sec., Mrs. Marguerite Cantrell, Box 1522, Santa Fe.

Oklahoma: *Examination.* Oklahoma City, Mar. 27-28. Exec. Sec., Mrs. L. Haidek, 813 Braniff Bldg., Oklahoma City.

Rhode Island: *Examination.* Providence, Feb. 18. Administrator of Professional Regulation, Mr. Thomas B. Casey, 366 State Office Bldg., Providence.

Texas: *Examination.* April 1959. Certificates issued by reciprocity and waiver on the first and fifteenth of each month. Sec., Bro. Raphael Wilson, 407 Perry-Brooks Bldg., Austin.

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*Basic Science Certificate required.

GOVERNMENT SERVICES

DEFENSE DEPARTMENT

Forensic Pathology Registry.—A Registry of Forensic Pathology has been established at the Armed Forces Institute of Pathology, Washington, D. C. It will be the 24th component of the American Registry of Pathology, and it is under the sponsorship of the College of American Pathologists. The objective of the new registry is the collection of well-checked and well-documented medicolegal cases to be used as a reservoir for teaching and research. Only selected cases of medicolegal interest contributed by a qualified pathologist will be registered. The material will be incorporated in the files of the Armed Forces Institute of Pathology and become a part of its national collection of pathology.

Registry consultation on contributed cases will be limited to basic pathological changes and will not include medicolegal opinions which might involve Armed Forces Institute of Pathology staff members in court proceedings. Cases are now being accepted for registration. A six-month fellowship in forensic pathology at the Armed Forces Institute of Pathology has been provided by the college as a part of its sponsoring support.

Aviation Pathology Committee Elects New Officers.—Officers for 1959 have been elected by the Joint Committee on Aviation Pathology, which held its fifth business meeting in December at the Armed Forces Institute of Pathology. They are Capt. Carl E. Wilbur, M. C., U. S. Navy, chairman, and Capt. Murray W. Ballenger, M. C., U. S. Navy, secretary. The committee, which includes medical officers of the military services of the United States, the United Kingdom, and Canada, uses the institute as the central coordinating facility for investigating the pathology of fatal aircraft accidents. Captain Wilbur, who is head of the Aviation Medicine Safety and Flight Training Branch, Bureau of Medicine and Surgery, Navy Department, Washington, D. C., will replace Col. Frank M. Townsend, M. C., U. S. Air Force deputy director of AFIP, as chairman. Captain Ballenger, who is on duty at the Armed Forces Institute of Pathology, will replace as secretary another staff member, Fathollah K. Mostofi, M. D., scientific director of the American Registry of Pathology.

AIR FORCE

Consultants Visit Medical Installations Abroad.—Drs. Garfield G. Duncan and Edgar J. Poth, national consultants to the Air Force surgeon general, recently visited medical installations in Germany, France, England, and Spain. They provided advice on problem cases in their respective specialities and conducted lectures and teaching sessions at medical installations. Doctor Duncan, of the Pennsylvania Hospital in Philadelphia, is a national consultant in internal medicine, and Doctor Poth, of the University of Texas Medical Branch in Galveston, is a national consultant in surgery.

VETERANS ADMINISTRATION

New Hospital Building at Fort Meade.—The VA Hospital at Fort Meade, S. D., occupies a new 60-bed combined medical, surgical, and administrative building Dec. 8, 1958. Fort Meade is a 720-bed neuropsychiatric hospital located 30 miles north of Rapid City on the site of a former U. S. Cavalry Post established soon after the Battle of the Little Bighorn. Fort Meade was garrisoned by Gen. George Custer's former regiment, the Fourth Cavalry, for many years. The new hospital building which provides beds for psychiatric patients with acute medical and surgical problems is the first phase of a long range construction program which will eventually replace all present bed facilities now housed in converted Army barracks.

New hospital at Fort Meade, S. D.

PUBLIC HEALTH SERVICE

Multiple Sclerosis Leaflet.—Recent developments in research on multiple sclerosis are described in a leaflet entitled "Multiple Sclerosis—Hope Through Research." One of the recent advances reported in the leaflet is a new understanding of myelin through biochemical research. Scientists have now discovered the specific manner in which one of the essential compounds of myelin, sphingosphine, is formed in the body and are now able to produce this substance in the laboratory. This new development may lead to additional knowledge concerning the disappearance of myelin and the possible reversal of this process. Prepared by the National Institute of Neurological Diseases and Blindness, National Institutes of Health, the leaflet is listed as Public Health Service publication no. 621 and Health Information series no. 92. Single free copies may be obtained from the National Institute of Neurological Diseases and Blindness, Bethesda 14, Md. The leaflet may be purchased in quantity from the Superintendent of Documents, Government Printing Office, Washington 25, D. C., at $3 for 100 copies.

DEATHS

Angeloni, Tito Ⓜ Providence, R. I.; Regia Università di Napoli Facoltà di Medicina e Chirurgia, Italy, 1905; died in Rocchetta al Volturno, Italy, Oct. 10, aged 79.

Bachulus, Matthew John Ⓜ Springfield, Mass.; Harvard Medical School, Boston, 1932; fellow of the American College of Surgeons; on the courtesy staff, Wesson Memorial Hospital; served on the staffs of the Westfield (Mass.) State Sanatorium, and the Springfield Hospital, where he died Oct. 27, aged 56.

Baxter, Harry Toler Ⓜ Astoria, Ill.; University of Illinois College of Medicine, Chicago, 1914; died in the Graham Hospital, Canton, Oct. 14, aged 66.

Becker, Charles Frederick Ⓜ Camden, N. J.; Jefferson Medical College of Philadelphia, 1953; member of the staff of Cooper Hospital; found dead in bed Oct. 28, aged 33.

Bellantoni, Raphael, Tuckahoe, N. Y.; Long Island College Hospital, Brooklyn, 1924; fellow of the American College of Surgeons; an associate member of the American Medical Association; director of obstetrics at the Union Hospital in New York City; consultant at the St. Joseph's Hospital in Yonkers and the Harlem Hospital in New York City; died Oct. 28, aged 59.

Blauvelt, John Hudson, Nyack, N. Y.; Cornell University Medical College, New York City, 1911; member of the American Psychiatric Association and the Industrial Medical Association; served on the staff of the Matteawan State Hospital in Beacon; died Oct. 31, aged 69.

Braun, Robert Frederick, Wausau, Wis.; Marquette University School of Medicine, Milwaukee, 1915; veteran of World War I; died Oct. 13, aged 74.

Broughton, George Anthony, La Jolla, Calif.; Medical Department of the University of California, San Francisco, 1896; an associate member of the American Medical Association; fellow of the American College of Surgeons; died Oct. 20, aged 83.

Bryan, Charles Silas Jr. Ⓜ Oakland, Calif.; Harvard Medical School, Boston, 1937; certified by the National Board of Medical Examiners; specialist certified by the American Board of Radiology; member of the American College of Radiology; veteran of World War II; clinical instructor of radiology at Stanford University School of Medicine in San Francisco; formerly on the staff of the Truesdale Hospital in Fall River, Mass.; associate radiologist at the Peralta Hospital; died Oct. 28, aged 47.

Burner, George Washington, Johnstown, Ohio; Columbus Medical College, 1892; veteran of World War I; for 10 years postmaster at Johnstown; died in Marysville Oct. 15, aged 95.

Carman, James Edwin, La Canada, Calif.; University of Minnesota College of Medicine and Surgery, Minneapolis, 1901; for many years practiced in Detroit Lakes, Minn.; died in the Elwood Sanitarium in Pasadena, Oct. 17, aged 80.

Crawford, William Shell, Tulsa, Okla.; Medical College of South Carolina, Charleston, 1914; served as a captain in the medical corps of the U. S. Army; for 26 years medical director of the Carter Oil Company; died Oct. 15, aged 67.

Deal, William Floyd Ⓜ Craig, Colo.; University of Nebraska College of Medicine, Omaha, 1919; on the staffs of St. Luke's Hospital in Denver and Memorial Hospital; died Oct. 22, aged 65.

Derr, John Sebastian Ⓜ Frederick, Md.; University of Virginia Department of Medicine, Charlottesville, 1905; specialist certified by the American Board of Radiology; fellow of the American College of Physicians; member of the American Roentgen Ray Society, Radiological Society of North America, and the American College of Radiology; from 1906 to 1908 a medical missionary in British West Africa; veteran of World War I; died Oct. 23, aged 77.

Dodd, Wilson Farnsworth Ⓜ Pleasant Hill, Tenn.; Cornell University Medical College, New York City, 1920; fellow of the American College of Surgeons; for many years a medical missionary in Turkey; during World War II was appointed medical director of the Near East Foundation in Greece; formerly medical director of the Berea (Ky.) College; on the staff of the Uplands Cumberland Mountain Sanatorium; died Oct. 30, aged 65.

Duncan, Owsley Bennett Ⓜ Paterson, N. J.; Columbia University College of Physicians and Surgeons, New York City, 1904; veteran of World War I; on the staff of the Barnert Memorial Hospital; died Oct. 15, aged 81.

Edwards, Aaron Robinson Ⓜ Ann Arbor, Mich.; Cornell University Medical College, New York City, 1938; interned at the Harper Hospital in Detroit; served a residency at the Children's Hospital

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Ⓜ Indicates Member of the American Medical Association.

in Detroit and the University Hospital in Ann Arbor, Mich.; specialist certified by the American Board of Pediatrics; member of the American Academy of Pediatrics; veteran of World War II; on the staffs of the Beyer Memorial Hospital, Ypsilanti, and St. Joseph Mercy Hospital; aged 46; died Nov. 9.

Franklin, Samuel Nathan Ⓜ West Allis, Wis.; Marquette University School of Medicine, Milwaukee, 1916; formerly county coroner; died in the Mount Sinai Hospital Oct. 14, aged 76.

Frost, Horace Bird, Lavonia, Ga.; Harvard Medical School, Boston, 1896; died in the Stephens County Hospital, Toccoa, Oct. 18, aged 87.

Gale, Eugene Manson, Merrimac, Mass.; College of Physicians and Surgeons, Boston, 1914; member of the Massachusetts Medical Society; served in France during World War I; on the staff of the Amesbury (Mass.) Hospital, where he died Oct. 23, aged 67.

Geraghty, Francis Joseph Ⓜ Baltimore; University of Maryland School of Medicine and College of Physicians and Surgeons, Baltimore, 1926; assistant professor of medicine at his alma mater; specialist certified by the American Board of Internal Medicine; fellow of the American College of Physicians; past-president of the Baltimore City Medical Society, of which he was a member of the executive committee; president of the staff and chief of medicine at the Bon Secours Hospital; on the staffs of the Mercy, Union Memorial, and University hospitals; died Nov. 1, aged 60.

Goldrick, Harold, New York City; University of Kazan Faculty of Medicine, Russia, 1919; on the staff of the New York Polyclinic Medical School and Hospital; died Oct. 26, aged 65.

Goodrich, Joseph Albert, Glenwood, Iowa; Northwestern University Medical School, Chicago, 1905; died Oct. 13, aged 85.

Guthrie, Donald Ⓜ Sayre, Pa.; born in Wilkes-Barre, June 23, 1880; University of Pennsylvania Department of Medicine, Philadelphia, 1905; emeritus professor of clinical surgery at the University of Pennsylvania Graduate School of Medicine in Philadelphia; professor, division of surgery, Hahnemann Medical College and Hospital of Philadelphia; gave the Ernest A. Sommer Memorial Lecture in Portland, Ore., in 1941 and the Mayo Lecture, University of Michigan, Ann Arbor, in 1954; in 1932 member of the House of Delegates of the American Medical Association; past-president of the Medical Society of the State of Pennsylvania, of which he was a councilor and trustee; past-president of the Alumni Association of the Mayo Foundation, Bradford County Medical Society, and the New York and New England Railroad Surgeons; member of the American Surgical Association, Surgical Research Society, Southern Surgical Association, American Association for the Surgery of Trauma, International Society of Surgeons, Royal Academy of Medicine, Rome, Conference, Board of Physicians in Industry, American Goiter Association, Royal Medical Society, Budapest, and the Association of Railroad Chief Surgeons; honorary member of the Society of Medicine and Surgery, Rio de Janeiro; fellow, and from 1930 to 1952 a member of the board of governors of the American College of Surgeons; member of the founders group of the American Board of Surgery; in 1937 received the honorary doctor of science degree from the Lafayette College, Easton, Pa.; on June 14, 1956, at the 109th annual commencement exercises of the Hahnemann Medical College and Hospital of Philadelphia, was awarded the honorary degree of doctor of humane letters; received an alumni award of merit in January of this year from the General Alumni Society of the University of Pennsylvania in recognition of outstanding service to the university; member of the surgical staff, Mayo Clinic, Rochester, Minn., from 1906 to 1909; served on the advisory board, *American Journal of Surgery;* for many years chief surgeon of the Lehigh Valley Railroad; founder of the Guthrie Clinic and chief surgeon of Robert Packer Hospital, where he died Oct. 30, aged 78.

Heck, Charles Christian Ⓜ Syracuse, N. Y.; University of Rochester School of Medicine and Dentistry, Rochester, N. Y., 1933; member of the Industrial Medical Association; veteran of World War II; physician for the state athletic commission; served as medical director of the Syracuse University athletic department; member of the staff of St. Joseph's Hospital, where he served an internship; died Oct. 30, aged 54.

Hedrick, Thomas Wade Ⓜ Abilene, Texas; University of Texas School of Medicine, Galveston, 1916; fellow of the American College of Surgeons; on the staffs of St. Ann Hospital, Cox Memorial Hospital, and the Hendrick Memorial Hospital, where he died Oct. 21, aged 67.

Hillis, Albert Edward Ⓜ Tacoma, Wash.; University of Michigan Department of Medicine and Surgery, Ann Arbor, 1902; specialist certified by the American Board of Otolaryngology; fellow of the American College of Surgeons; past-president of the Pierce County Medical Society; on the staff of the Northern Pacific Beneficial Association; charter member of the Tacoma Lions Club; died in South Pasadena, Calif., Oct. 24, aged 84.

Horstman, Frank Marion, Northbrook, Ill.; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1904; also a graduate in pharmacy; formerly on the faculty of his alma mater and the Loyola University School of Medicine in Chicago, where he served as a member of the council; for many years on the staff of the McKinley High School in Chicago; for three years an examining physician for the Chicago, Burlington, and Quincy Railroad; formerly associated with the Augustana Hospital in Chicago; died Oct. 27, aged 80.

Huey, William, Seattle; University of Edinburgh Faculty of Medicine, Scotland. 1939; died Oct. 24, aged 45.

Hutchinson, Claribel Merrill, Pasadena, Calif.; Woman's Medical College of the New York Infirmary for Women and Children, New York City, 1887; died Oct. 26, aged 100.

Jeppson, John Rufus Ⓜ New Rochelle, N. Y.; Jefferson Medical College of Philadelphia, 1923; on the staff of the New Rochelle Hospital; died Nov. 2, aged 62.

Jones, Milton Easley Ⓜ Ocean City, Md.; University of Maryland School of Medicine and College of Physicians and Surgeons, Baltimore, 1915; member of the American Urological Association and the Ohio State Medical Association; formerly practiced in Columbus, Ohio, where he was associated with Mount Carmel and Grant hospitals; died in the Peninsula General Hospital, Salisbury, Oct. 21, aged 70.

Kinnamon, Frank Ⓜ Concordia, Kan.; Kansas Medical College, Medical Department of Washburn College, Topeka, 1912; county coroner and health officer; for 12 years member of the board of education; on the staff of St. Joseph's Hospital, where he died Oct. 9, aged 78.

Kohler, Delphin William Ⓜ Tacoma, Wash.; John A. Creighton Medical College, Omaha, 1916; member of the American Academy of General Practice; service member of the American Medical Association; veteran of World War I; retired from the Veterans Administration Aug. 1, 1955; formerly on the staff of the Veterans Administration Hospital in American Lake; died Oct. 28, aged 70.

Kolettis, George John Ⓜ Gary, Ind.; National University of Athens School of Medicine, Greece, 1915; died in St. Mary's Mercy Hospital Aug. 27, aged 64.

Lahn, Louis Ⓜ Great Neck, N. Y.; born in Norwich, Conn., Aug. 22, 1895; Fordham University School of Medicine, New York City, 1921; specialist certified by the American Board of Obstetrics and Gynecology; adjunct professor of gynecology and obstetrics at the New York Polyclinic Medical School and Hospital; associate in obstetrics and gynecology at the New York Medical College, Flower and Fifth Avenue Hospitals; fellow of the American College of Surgeons and the International College of Surgeons; practiced in New York City, where he was associated with the Flower and Fifth Avenue Hospitals, Hospital for Joint Diseases, Metropolitan Hospital, and the Bird S. Coler Hospital; died in the William W. Backus Hospital, Norwich, Conn., Oct. 30, aged 63.

Lape, Charles Pearley, Buffalo; Hahnemann Medical College and Hospital of Philadelphia, 1909; member of the Medical Society of the State of New York; specialist certified by the American Board of Radiology; a charter member of the Buffalo Radiological Society; served on the staff of the Millard Fillmore Hospital; died in Portland, Maine, Oct. 13, aged 75.

MacLiesh, Henry, Brooklyn; Medizinische Fakultät der Universität, Vienna, Austria, 1925; on the staff of the Unity Hospital and Adelphi Hospital; died in the Mount Sinai Hospital, New York City, Aug. 3, aged 57.

McCuskey, John Fulton Ⓜ Clarksburg, W. Va.; born in Hingham, Mass., April 6, 1910; Northwestern University Medical School, Chicago, 1937; specialist certified by the American Board of Urology; member of the American Urological Association and the Southern Medical Association; from 1953 to 1956 a member of the council of the West Virginia State Medical Association; fellow of the American College of Surgeons; past-president and secretary of the Harrison County Medical Society; during World War II was assigned to the 106th Station Hospital and served in Italy, Okinawa, and Japan; released from the service in 1946 with the rank of lieutenant colonel; past-president of the staffs of St. Mary's and Union Protestant hospitals; aged 48; died Oct. 30.

Marra, Frank Paul Ⓜ Schenectady, N. Y.; Albany (N. Y.) Medical College, 1927; member of the American Academy of General Practice; served as city councilman; died Oct. 25, aged 54.

Monroe, Alvin Henry, Elmira, N. Y.; Syracuse University College of Medicine, 1909; an associate member of the American Medical Association; served as medical examiner for the Chemung County Draft Board during World Wars I and II and served as health officer for the town of Southport; for many years county coroner; associated with the Arnot Ogden and St. Joseph's hospitals; died Oct. 23, aged 77.

O'Malley, William P., Milwaukee; University of Wisconsin Medical School, Madison, 1928; member of the American Academy of General Practice; veteran of World War I; past-president of the Wauwatosa Kiwanis Club; on the staff of the Milwaukee Hospital; died Oct. 28, aged 60.

Op de Beeck, Fernand G. P., Montvale, N. J.; Universteit Gent Faculteit der Geneeskunde, Belgium, 1902; died Sept. 3, aged 83.

Ostfield, E. Vaughn, Pittsburgh; University of Pittsburgh School of Medicine, 1958; intern at the Presbyterian Hospital; found dead at her summer cottage near Confluence Dam, Sept. 28, aged 29.

Paul, Robert Clifford Ⓜ Wooster, Ohio; University of Wooster Medical Department, Cleveland, 1892; served on the draft board during World Wars I and II; past-president and secretary of the Wayne County Medical Society; on the staff of the Wooster Community Hospital; died Oct. 28, aged 97.

Powers, Edward Sharp Ⓜ North Hollywood, Calif.; Washington University School of Medicine, St. Louis, 1935; veteran of World War II; associated with St. Joseph Hospital in Burbank and the Good Samaritan Hospital in Los Angeles; died at the International Airport in Inglewood Oct. 23, aged 50, while awaiting a plane for a vacation trip to Mexico.

Robison, E. Waid, Dallas, Texas; Baylor University College of Medicine, Dallas, 1926; veteran of World War II; served on the staffs of the Veterans Administration hospitals in Waco and Bonham; associated with the Taylor Clinic; aged 59; died Oct. 8.

Schauffler, Robert McEwen Ⓜ Kansas City, Mo.; Columbia University College of Physicians and Surgeons, New York City, 1896; formerly on the faculty of the University of Kansas School of Medicine in Kansas City, Kan.; past-president of the Jackson County Medical Society; member of the American Orthopaedic Association, Clinical Orthopaedic Society, and the American Academy of Orthopaedic Surgeons; fellow of the American College of Surgeons; for many years on the staff of the Children's Mercy Hospital; died in the Research Hospital Oct. 30, aged 87.

Seibert, Daniel Glenn, Jackson, Mo.; Vanderbilt University School of Medicine, Nashville, Tenn., 1901; for many years on the school board; died in the Southeast Missouri Hospital, Cape Girardeau, Oct. 3, aged 81.

Smith, Thomas Elmo Ⓜ Independence, Kan.; Kansas City (Mo.) Medical College, 1904; served as a member of the state legislature; vice-president and director of the Independence State Bank; on the staff of the Mercy Hospital, where he died Oct. 21, aged 80.

Sturdivant, Burton Barrett, West Union, W. Va.; Maryland Medical College, Baltimore, 1912; county health officer; during World War I was a member of the medical corps of the U. S. Army and served overseas as regimental surgeon of the 540th engineers with the rank of captain; died in Winston–Salem, N. C., Oct. 31, aged 71.

Van Arsdall, Condit Brewer Ⓜ Harrodsburg, Ky.; Johns Hopkins University School of Medicine, Baltimore, 1902; for many years served on the board of education and 14 years as chairman; served as president and secretary of Mercer County Medical Society; for many years president of the Harrodsburg Historical Society; served eight years as a member of the board of directors of the Good Samaritan Hospital in Lexington; member of the staff and board of trustees of the James B. Haggin Memorial Hospital, where he died Oct. 25, aged 83.

Whetstone, Adair K. Ⓜ Sylacauga, Ala.; Birmingham Medical College, 1914; received the Good Citizenship citation of the Civitan Club; voted "Man of the Year" by the Chamber of Commerce; on Aug. 2, 1953, Sylacauga observed "Dr. Whetstone Day" to pay tribute to him for his service to this section; church services as well as a city-wide afternoon meeting honored him and at that time three Dr. Whetstone Scholarships were established for the Sylacauga Hospital School of Nursing; on the staffs of the Drummond Fraser Hospital and the Sylacauga Hospital, where he died Oct. 19, aged 80.

Wilson, Harry Franklin Ⓜ Columbia, S. C.; born in Bowman Aug. 23, 1904; Medical College of South Carolina, Charleston, 1928; veteran of World War II and was awarded the American Defense, Armed Forces Reserve, American Theater, Asiatic–Pacific Theater with two battle stars, Victory, Occupational (Japan), and the Philippine Liberation campaign ribbons for Army service; in 1951 was awarded the Cross of Military Service of the United Daughters of the Confederacy; since 1949 director of the division of laboratories of the state health department and formerly served as director of industrial health; formerly health officer of Horry County, Beaufort County, and the Dillon–Marion Health District; died in the Veterans Administration Hospital Oct. 23, aged 54.

Woodcock, Lee Barnes, Sedona, Ariz.; Medico-Chirurgical College of Philadelphia, 1898; died Oct. 24, aged 87.

Woods, Ernest Arthur Ⓜ Ashland, Ore.; University of Minnesota College of Medicine and Surgery, Minneapolis, 1899; specialist certified by the American Board of Otolaryngology; past-president and secretary of the Southern Oregon Medical Society; past-president of the Jackson County Medical Society; formerly member of the council of the Oregon State Medical Society; served as a member of the city council; company surgeon for Southern Pacific Railroad; served on the staff of the Community Hospital; died Oct. 12, aged 83.

Wylie, Robert Lawson Ⓜ Scotts Hill, Tenn.; University of Tennessee Medical Department, Nashville, 1906; for 46 years president of the Farmers State Bank; on Oct. 14, 1950, honored on "Dr. Wylie Day" and his friends presented him with a new automobile; died Oct. 11, aged 81.

FOREIGN LETTERS

AUSTRIA

Iron-Deficiency Anemia.—At the meeting of the Society of Physicians in Vienna on Nov. 7, Drs. A. Stacher and J. Böhnel said that iron tablets do not always agree with the patients and are not always absorbed properly. Intravenous injections sometimes cause thrombosis and other side-effects. They treated a series of 47 patients, of whom 17 had essential hypochromic anemia, 16 posthemorrhagic anemia, 9 anemia caused by infection and tumors, and 5 postoperative anemia with intramuscularly administered iron-dextran complex (Myofer) and found that the hematopoietic effect of the drug was equal to that of intravenous injections. These results were corroborated in some patients by constant control of the iron content in the serum. In patients with anemia caused by infections or tumors in whom no concomitant true iron-deficiency due to hemorrhages was present, no significant improvement could be achieved while the other types of iron-deficiency anemia showed excellent remissions with the intramuscular treatment.

Treatment of Neuralgia.—A the same meeting Dr. F. Bodart reported on a series of 28 patients with neuralgia due to involvement of nerve roots, chiefly sciatica, whom he treated with intrathecal injections of prednisolone. Nine of the patients became free from pain and remained so. In the rest the reaction was of short duration. Meningism as a side-effect sometimes occurred. This treatment was considered a valuable addition to the measures hitherto used.

Dissemination in the Course of Eczema.—At the same meeting Dr. W. Lindemayr reported on the clinical aspect and the course of the dissemination reaction observed in 100 patients with generalized eczema which had spread from an initially circumscribed lesion. On the basis of intracutaneous and epicutaneous tests with bacterial and fungus allergens and epicutaneous tests with contact allergens which possibly have an additional effect, the speaker concluded that the dissemination reactions should be ascribed to an allergy against autoantigens. The evidence indicates that these autoantigens develop in the primary focus under the influence of bacteria and fungi.

Anemia and Geophagia.—At the meeting of the Society of Physicians in Vienna on Nov. 14, Dr. H. G. Weippl said that geophagia has long been of interest only to the psychiatrist, but it is coming to be of interest to roentgenologists and pediatric hematologists as well. Four children, their ages ranging from 1 to 2 years, with geophagia and severe hypochromic anemia were observed. Thorough examination, especially of the serum iron level, revealed iron-deficiency as the cause of the anemia. When geophagia was no longer present and the children were given iron therapy, immediate improvement of the anemia was noted. Even without iron therapy a gradual improvement could be seen. The obsessive eating of abnormal objects is rare in Europe, and the geophagia in children of this age is considered a benign, temporary disturbance which does not reflect a disturbed mental development.

BRAZIL

Diagnosis of Syphilis.—At the meeting of the São Lucas Medical Society of São Paulo in October, Dr. Luiz Migliano reported that a series of 523 positive Migliano microreactions agreed with the results of the standard and presumptive Kahn test on the same serums, and a series of 16,761 negative reactions agreed with the results of Kahn, Meinik, and Wassermann tests. The simplicity of the technique of the Migliano's reaction and the fact that a minimum of material is necessary for its performance makes it of great use for routine examinations.

Operations for Pelvic Cancer.—Dr. Azael Leistner (*Revista de medicina e cirurgia de São Paulo,* July, 1958) performed 15 pelvic exenterations (10 total and 5 partial) for carcinoma of the uterine cervix, vulva, rectum, and bladder, with local metastases to the lymph nodes. Most of the patients had been previously operated on or had received roentgen and radium therapy with unsatisfactory results. Dr. Leistner made 13 temporary cutaneous ureterostomies (he does not advise ureterosigmoidostomies because of the danger of stenosis, infection, and acidosis), 2 ileocecal bladder reconstructions, and 1 ureteroileosigmoidostomy, which should be performed in patients in whom the cancer is supposedly cured. The total volume of whole blood used during the operation was from 1.5 to 3.8 liters. In one patient he suspended the bladder and made the abdominopelvic separation with a graft of the fascia lata, with excellent results. In another, he peritonealized the pelvis suturing the anterior parietal peritoneum to the posterior peritoneum. There were five deaths in the late postoperative period

(3rd, 4th, 5th, and 10th months) and seven in the immediate postoperative period. One patient was in good condition when last seen 6 months after operation and another 23 months after operation. The adverse results were probably due to the fact that in many cases the operation was done for palliative reasons (in patients with urinary and fecal fistulas). The author believed that the operation should be done only when there is adequate equipment and a well-trained surgical staff.

Surgical Treatment of Goiter.—Dr. R. A. Santos (*Revista paulista de medicina*, vol. 53, 1958) operated on 303 patients with thyroid diseases; 185 (61.1%) with simple goiter, 110 (36.3%) with toxic goiter, 4 (1.3%) with tuberculous thyroiditis, and 4 with other conditions. Of the 50 patients whose basal metabolism was determined, in 33 with diffuse toxic goiter the metabolic rate averaged 128, and in 17 with nodular toxic goiter the rate averaged 130. The patients with diffuse goiter presented the highest and the lowest increases in metabolic rate, since the hyperthyroidism of this type of goiter responds rapidly to chemical treatment and several patients had undergone previous medical treatment with iodine. Further spontaneous remissions may occur.

In the 110 patients with toxic goiter, 111 operations were performed. There were three deaths, or a fatality rate of 2.7%, and several patients presented complications. Three suffered a thyrotoxic crisis in the immediate postoperative period. One of these patients who had been operated on before the introduction of the hibernotherapy died, and another, treated by hibernation, recovered promptly from a thyrotoxic crisis. The third patient of this group died a few hours after operation. Tetany occurred in only one patient (on the fifth day after the operation), the crisis having been successfully treated with only calcium and vitamin D. The author believes that, as a rule, no other drugs are needed. Chvostek's and Trousseau's signs were not looked for, the first being almost always present in the first days after operation and therefore without special significance. Hyperthyroidism in the last postoperative period occurred in four patients, one of whom had uncontrollable vomiting. Hyperthyroidism was much less frequent in patients with simple goiter—one case in the 185 patients. There was no case of aggravation of exophthalmus after the operation, but a few patients had slight hemorrhages.

Plastic Surgery of the Esophagus.—Dr. O. M. Dantas reported to the Associacão Paulista de Medicina a series of 16 patients with cancer of the esophagus in whom a total reconstruction of the organ was performed in 15 by using a portion of the colon and in one by using a portion of the stomach. In two patients whose tumor was situated in the lower third of the esophagus the route of access was a transdiaphragmatic thoracolaparotomy, but the author considers this a bad route, in view of the difficulties caused by the thoracopulmonary dynamics, mainly from the section of the diaphragm. From the technical standpoint this is a good route, as it widely exposes the lower third of the esophagus, permitting easy handling of the stomach and colon. For total esophagectomy, however, this route is unsuitable, since the separation of the esophagus at the level of and above the aortic arc causes dangerous reflexes. The placing of the colon in the thoracic cavity reduces the pulmonary capacity and causes compression of the left bronchus, hindering the elimination of secretions and favoring the occurrence of atelectasis. Too long an exposure of the pleural cavity with the lung collapsed favors the occurrence of pulmonary complications. These reasons led the author to abandon this route.

In three patients whose tumor was situated on the middle third of the esophagus, the operation was performed in two stages. In the first, a right thoracotomy, esophagectomy, closure of the thoracotomy, left laparotomy, distal section of the esophagus, gastrostomy, and cervical esophagostomy were accomplished. In the second a laparotomy for the closure of the gastrostomy, cologastroanastomosis, and left thoracotomy for the interposition of the colon with cervical colostomy were performed. As the interposition of the colon through the hemithorax was considered inconvenient, the author tunnelized the anterior mediastinum for the interposition of the colon. He believed that by this procedure the colon or the stomach, when placed in the anterior mediastinum, did not interfere with the function of the heart and the large vessels and was more easily tolerated by the lungs than when placed in the thoracic cavity. All the patients on whom this route was used had an uneventful postoperative course. The experience of the author with the mediastinal tunnelization led to its use for all esophageal tumors. It was even possible in several patients to perform the operation in one stage. From the point of view of the route of access, the author recommends tunnelization for the reconstruction of the esophagus. As complications of this procedure, abscess of the mediastinum, due to insufficient length of the colon and obstruction by compression of the colon against the sternal manubrium, were observed.

Labor After Previous Cesarean Section.—Dr. Martiniano Fernandes (*Revista de ginecologia e d'obstetricia*, vol. 52, 1958) reported a series of 1,515 deliveries by cesarean section. Of these, 210 patients had had a previous cesarean section and in 33 a trial of natural delivery resulted in dehiscence of the uterine scar. The good results of the transpelvic spontaneous deliveries observed in about 33% of the author's patients indicated the possibilities of a trial at labor provided the patients are carefully selected. Contraindications of such a test may be ascertained by hysterography performed four months after cesarean section to discover faults in the scar. As most of the patients in this series presented obstetrical emergencies, the maternal death rate was 15% and the fetal death rate was 39.3%. The following conditions should be fulfilled for the best treatment of such patients: (1) roentgenographic proof of fetopelvic compatibility, (2) an easily dilatable cervix, (3) vertex presentation, (4) engagement of the head in the cervical canal, (5) normal uterine dynamics, and (6) absence of pain in the region of the surgical scar during the uterine contractions. In such patients the performance of version by external maneuvers, extractions, the application of forceps except at the end of the delivery, use of oxytocics, and Kristeller's maneuver are definitely contraindicated.

FRANCE

Coronary Arteriography.—At a meeting of l'Académie Nationale de Médecine, C. Arnulf of Lyon stated that he was able to inject a contrast medium into the ascending aorta during the cardiac pause induced by acetylcholine and lasting about nine seconds. By this means he obtained excellent roentgenograms of the coronary arteries first in experimental animals then in man without any untoward effects. This procedure is of value in localizing damage to the coronaries prior to surgical treatment.

Bronchogenic Cancer.—F. Denoix and co-workers (*Bulletin de l'association Française pour l'etude du cancer,* vol. 45, 1958) analyzed a series of 602 patients with bronchogenic cancer. They confirmed the existence of a correlation between these cancers and smoking. Other factors included chronic bronchitis, poor oral hygiene, inhalation of poisonous gas in World War I (even among nonsmokers), and heavy consumption of coffee. It is not yet known whether the benzopyrine in coffee is responsible for an increased incidence of lung cancer in coffee drinkers.

Respiratory Allergies in Children.—R. Mande and co-workers (*Annales de pédiatrie,* July, 1958) studied the allergenic action of house dust. Sensitivity to house dust was observed even in infants 6 months old. It was manifested by spasmodic or catarrhal rhinitis, fits of coughing, and typical asthmatic attacks. It was aggravated by tonsillectomy. An eosinophilia of 4 to 20% was observed and eosinophils were found in the bronchial secretions. In a series of 154 children treated by desensitizing injections, 1.9% were not benefited, 11.7% obtained partial improvement, and 86.4% were completely relieved.

Suppurative Adenitis due to BCG Vaccine.—R. Mande and co-workers (*La revue de la tuberculose,* vol. 3, 1958) found that in a series of 29,898 persons vaccinated with BCG vaccine, 96 developed suppurative adenitis, 48 of whom were less than 2 years old. The lesions appeared three months after vaccination; 26 involved more than one node. There were no severe reactions and recovery occurred in two or three months without treatment. In the children under 2 this complication was seen less frequently in those vaccinated by scarification than in those vaccinated by intradermal injection.

INDIA

Dementia Paralytica.—A. V. Rao (*Current Medical Practice,* vol. 2, September, 1958) reported that 33 (or 5%) of 661 consecutive new patients admitted to the Government Mental Hospital in Madras in 1954-1955 had dementia paralytica and in 1956 the incidence of this disease among new admissions was 3%. Among the 33 patients the highest age incidence was in the third and fourth decade; 2 patients were over 50 and 1 was only 20. Eleven of the patients had been mental workers and 11 had been manual laborers; 16 had pupillary abnormalities, in 8 of whom the typical Argyll Robertson pupil was seen while in 7 others incomplete Argyll Robertson pupils were noted. In one patient the pupils were dilated. Two had chorioidoretinitis and two of the three patients with taboparesis had bilateral optic atrophy. Speech disturbances were present in 25 patients and consisted of slurring, anarthic mutism, nominal aphasia, palilalia, and echolalia. Twenty two of the patients had tremor of the tongue; 23 had tremor of the fingers; 4 developed convulsions; and hemiplegia was observed in 3. Associated tabes dorsalis was seen in three who also had Argyll Robertson pupils. Aural hematomas were seen in four patients. One had marked clubbing of the fingers in both hands. Two had spontaneous fractures involving both femurs due to osteoporosis and some had loss of weight. Only 11 had grandiose ideas and only 2 of these showed expansive megalomania. The simple demented type was seen in another 11; 5 showed acute maniacal excitement; 3 had chronic excitement; 2 showed depression; and 1 had auditory hallucinations. Loss of memory was common and so was insomnia. Four patients had Korsakoff's psychosis. Enlargement of the aortic shadow was seen in the chest roentgenograms of five patients. One had clinically recognizable aortic regurgitation and another had aneurysm of the ascending aorta. The spinal fluid gave a positive Wassermann reaction with a paretic type of colloidal gold curve in all patients. The blood and spinal fluid were serologically positive in 25.

UNITED KINGDOM

The Mind and the Machine.—The Nuffield Foundation has made a grant of $95,200 to the department of anatomy, University College, London, for the construction of a new computer which resembles the nervous system of an animal. This latest development in the study of the mind is based on the work of Prof. J. Z. Young on the learning mechanism of the octopus, which has remarkable ability to classify what it sees. Its skill in recognizing shapes depends on two sets of neurons that continually reactivate each other. If one set is put out of action, the octopus loses recent memories and only slowly learns any new classification, but its memory for old shapes is unaffected. It therefore seems that one of these sets forms the memory store, while the other is the printing device which inscribes new shapes on the memory. The arrangements by which the two parts are connected with each other have been worked out in detail. They involve several networks of nerve fibers, apparently a randomizing system allowing the possibility that each point in one lobe may be connected with any point in the next. It is to test these hypotheses that the new computer is to be built. It will consist of about 4,000 identical units, each of which will be an electronic analogue of a single neuron and its synaptic terminals. It is believed that in an animal information is stored at the synapses between neurons and that the receipt of nerve impulses changes the transmission power of the synapse. The units in the computer will be constructed to perform in the same way and thus give the computer a memory.

The networks will be trained to recognize shapes held in front of the computer's model eye. As each different shape is presented to the eye a different sound will be made in the machine's model ear. If the training is effective, the computer will be able to emit the appropriate sound when the shape is brought into its field of vision. It should also be within the range of the new computer to simulate the learning of the alphabet and the numerals and a limited number of more complex shapes which might even include human faces. The output stage will control the movement of levers that could simulate the movements of animals, the production of writing by man, or the generation of recognizable speech sounds. The computer should be finished by the end of 1960.

Trichomonal Vaginitis.—Of the compounds available for the local treatment of trichomonal vaginitis phenylmercuric dinaphthylmethane disulphonate is preferable to other preparations, being effective, free from toxic reactions, and acceptable to the patient, according to Murrell and Gray (*The Practitioner* 181:611, 1958). This conclusion is based on their findings in a series of 125 patients, in 118 (94%) of whom the vagina was microscopically cleared of trichomonads at some stage during the trial. In 72 patients (60%) swabs from the vagina were negative for trichomonas after two weeks. Relapses or reinfestations occurred in 70 patients (56%) on at least one occasion: 29 (23%) of these patients defaulted at least once. Clinically, the end-results were classed as good in 97 patients (78%) and poor or failures in the rest. No intolerance or local sensitivity was encountered in any of the patients treated. In patients with heavy infestation, the vagina was swabbed under direct vision with an aqueous solution of the drug. The patients were instructed to insert two pessaries of the drug high in the vagina every night for two weeks, but to return in one week for progress to be assessed. In most patients treatment was continued with one pessary nightly for a further minimum period of four weeks, increasing to two pessaries at menstrual periods. Only those with a clinical urethritis accompanied by a positive urethral smear were given local treatment of the urethra: 60 ml. of a urethral jelly containing 0.1% of the drug, introduced by means of a tube fitted with a suitable nozzle. This procedure was repeated when necessary at subsequent visits.

Recurrent Stys.—Recurrent stys should be treated by an antibacterial ointment applied to both the nose and eyes, according to P. W. M. Copeman (*Lancet* 2:728, 1958). This conclusion was based on the high incidence of Staphylococcus pyogenes var. aureus in the anterior nares of patients with recurrent stys. In a series of 18 patients with less than one sty a year, this organism was isolated from the nares in 8—an incidence of 44% of nasal carriers, which is similar to that in the general population. The comparable percentage in 36 patients with recurrent stys was 94. In most of these patients the application of a neomycin-bacitracin ointment to the nares was sufficient to break the run of stys, but in some it was also necessary to apply the ointment to the eyelids. It was therefore recommended that such an ointment be applied to the nares and the eyelids four times a day for 10 days, followed at biweekly intervals by courses of 7 days' treatment. This is frequent enough to prevent recolonization of the nares.

Physicians' Cathedral Window.—The Guildford division of the British Medical Association is appealing to the profession for contributions to a fund to provide one of the windows in the new Guildford cathedral, the nave of which is now nearing completion. It is believed that American physicians who served in or around Surrey in World War II may wish to participate in this gracious gesture. Donations should be sent to the Doctors' Cathedral Window Fund, c/o The Treasurer, Dr. F. A. Belam, 1 Westfield, Epsom Road, Guildford, Surrey.

MISCELLANY

REPORT ON CONFERENCE ON STAPHYLOCOCCIC DISEASE

The National Conference on Staphylococcal Disease, co-sponsored by the United States Public Health Service and the National Research Council, which met in Atlanta, Ga., headquarters of the Communicable Disease Center, Sept. 15-17, was attended by delegates from 59 professional organizations and numerous authorities on various aspects of the infection problem.

In the opening address, Dr. Leroy E. Burney, surgeon general of the Public Health Service, said that the purpose of the meeting was to review what is known about and to recommend what can be done to control staphylococcic infections which are acquired by hospital patients. These infections do not respond to the penicillin and other antibiotic drugs that kept them under control until recently.

The conference delegates agreed that the drug-resistant infection is now a problem in practically all hospitals throughout the world. Serious epidemics, although infrequent, have occurred unexpectedly in many hospitals.

Usually starting in surgical wards and in nurseries for newborn infants, the disease is spread through the hospital and out into the community by these patients, many of whom show no symptoms, such as boils and abscesses, until after they leave the hospital. Fear of causing public alarm which might deter persons from getting needed hospital care has caused some hospitals to attempt to hide their problem. However, hospital administrators who attended the conference reported a growing awareness that open recognition of the problem will contribute to its control.

Because staphylococcus germs are ubiquitous and because the drug-resistant strains permeate hospitals and their personnel, the prevention of serious infection, the delegates agreed, is a matter of finding how the dangerous strains are spread and building barriers against them. Although the delegates recognized that contaminated air and furnishings could be responsible for spreading the infection, the prevailing opinion was that personal contact is one of the most common causes. Most of their recommendations were therefore concerned with reducing this cause.

Their major recommendations included the following:

1. Organization of infection-control committees in all hospitals. These committees should have sufficient authority to investigate infections and establish and enforce hospital policies. They should include representatives from all services and divisions, all of whom should have a keen interest in the problem and should meet at regular and frequent intervals. Committee members should be responsible for seeing that hospital personnel are properly trained in anti-infection procedures and that these procedures are followed in daily activities. Local health officials should be asked to serve as consultants to these committees. The organization of infection-control committees by local medical societies, with representatives from the medical, nursing, and housekeeping staffs of all the hospitals in the area, was considered a necessary supplement to the intrahospital committee.

2. Use of an "infection log" in which all infections would be classified and pertinent data recorded. This would make it possible to determine whether infections are increasing and would also help the control committee to evaluate the effectiveness of its measures.

3. A plan for excluding from contact with patients all personnel who have boils or other active staphylococcic lesions or who are known to be carriers of dangerous and epidemic strains. Periodically, in nurseries for the newborn and at times of epidemics in other areas of the hospital, cultures should be made from personnel in order to detect, remove, and treat dangerous carriers. During epidemics, persons found to be carriers of dangerous epidemic strains should be removed from contact with patients until they are free from infection.

4. A local plan for establishing criteria for the discriminate use of antibiotics in medical and surgical treatment. Prophylactic use of antibiotics was considered highly undesirable.

5. Arrangements to store cultures from staphylococcic infections. This would help the hospital to trace the source of an epidemic if one should occur. The length of time these cultures should be stored would be decided by the infection-control committee.

6. Isolation of infectious patients, particularly those with pulmonary and skin infections, even if this means expanding isolation facilities. More emphasis on home care, in preference to hospitalization, was also suggested for patients with minor illnesses or with diseases that make them particularly vulnerable to staphylococcic infection. Diagnostic and treatment procedures in the hospital

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A symposium on staphylococcic infections was published in The Journal March 8, 1958, page 1177.

was associated with it—which is the normal barrier to [illegible]ection—should be kept to a sensible minimum.

7. Special precautions in nurseries for newborn infants, such as elimination of overcrowding and maintenance of rigid sanitary standards. Bathing babies immediately after birth with an antiseptic such as hexachlorophene was also recommended. Since babies are the principal source of spreading the disease into the community, sample surveys of families at periodic intervals after their babies have been discharged from the hospital were advised. Such surveys can be made by telephone, mail questionnaire, or home visit. Early detection of nursery-acquired infection would help to prevent further spread. These surveys would also indicate whether the hospital had an infection problem which it had not recognized because of the late appearance of symptoms.

8. Development of intensive and continuous training programs for professional and subprofessional members of hospital staffs. To aid in these programs, the delegates recommended that the American Hospital Association, the American Medical Association, and the Public Health Service collaborate in producing and distributing training films and other educational materials. They also proposed that the Public Health Service produce and distribute widely to hospitals a manual containing all available information on environmental disinfection and on the sterilization of equipment, linen, and other objects used with patients.

9. Strengthening of laboratory services. By the phage typing process, it is possible to identify dangerous strains of staphylococcus and thus enable hospitals to trace the source of infection. However, since it is not practical for many institutions to do this, it was recommended that the Public Health Service, through its own facilities and by assisting state and local health department laboratories, should aid in performing phage studies, particularly in epidemic situations.

10. Expansion of research. Areas in which the delegates felt more knowledge was needed before recommendations could be made included (1) the effect of environmental contamination on the spread of infection; (2) desirable features in the design and construction of hospitals and hospital equipment, as the delegates believed that not enough is known about environmental factors in the spread of infection to warrant recommending extensive or expensive changes in existing structures; (3) the value of making staphylococcic infection a reportable disease. (Several states now require reports on all such cases and results in these states will be studied.)

The group also issued strong recommendations for basic research to determine why some people are more susceptible to infection than others and how a person's resistance to it can be strengthened, and also to find better methods of treating diseases caused by virulent and epidemic strains and ways of minimizing the development of drug-resistant strains.

Dr. Burney pledged the Public Health Service to do everything within its power to put these and other recommendations made by the conference into effect. The Public Health Service has already taken action on several of these measures. Applications for grants to carry on research on staphylococcic infections are being given priority consideration by the Advisory Councils of the National Institutes of Health and, through a special appropriation of one million dollars ear-marked for the study of staphylococcic infection, grants will be made this fall to support the most promising projects.

To assist states and communities in the rapid identification of epidemics, the Communicable Disease Center is preparing diagnostic reagents on a large scale. The Center has also assumed responsibility for operating the National Reference Center for Staphylococcal Phage Typing. Through its Epidemic Intelligence Service, the Center makes available specially trained physicians and nurses to help trace the source of epidemics and bring them under control. Training programs for laboratory and other personnel of state and local health departments have also been expanded by the Center.

Highlights of some other papers presented at the conference are as follows: Dr. R. Keith Cannan, chairman of the Division of Medical Sciences of the National Research Council, co-sponsor of the conference, explained that the council's interest in the problem stemmed from its study of the treatment of traumatic injuries, particularly burns.

Dr. R. E. O. Williams of the Public Health Laboratory Service, London, described the experience of the British, who were the first to isolate antibiotic-resistant strains of staphylococcus. He reported sample surveys in England which indicate that, apart from epidemics, about 5% of clean wound operations and 10 to 15% of newborn babies develop septic lesions. Describing the "wound books" which some English hospitals maintain on all operations, he said, "It is our feeling that systems which simply require notification of cases of infection are less likely to give complete records than those that demand recording of the outcome whether infection develops or not." He also advocated painting the umbilical stumps of newborn babies, a frequent site of infection, with antiseptic dye. Summarizing these and other English practices, he said, "There is no one way in which staphylococci spread in a hospital and there is no one prophylactic method by which spread can be prevented. The routes of infection are numerous and probably often devious and the precautions needed are many and complex. . . . Our preventive measures have therefore to minimize the endemic level, to prevent the emergence of epidemics, and to terminate epidemics when they occur."

Dr. Robert J. Anderson, chief, Communicable Disease Center, Atlanta, cited the provision of adequate laboratory service, staffed by well-trained bacteriologists and technicians, within the hospital and at all levels of organized public health as a major need that must be met in order to apply the best available methods of controlling the disease. Noting that the indiscriminate use of antibiotics in medical treatment has been deplored by clinicians for years, he said, "The time is perhaps ripe for the positive approach—the formulation and promulgation of acceptable standards for the discriminate use of antibiotics."

Dr. Vernon Knight, associate professor of medicine, Vanderbilt University School of Medicine, Nashville, Tenn., described studies which indicated that, after patients have been in the hospital for a few days, the staphylococcic strains which they normally carry on their skins or in their noses are replaced by the drug-resistant strains which prevail in the hospital environment. After discharge from the hospital, the process reverses, with the normal strains replacing the drug-resistant strains.

Dr. Thomas E. Shaffer, professor of pediatrics and preventive medicine, Ohio State University College of Medicine, Columbus, speaking on outbreaks of infections in nurseries, noted that they began about 12 years ago in England, subsequently occurred in Canada, Australia, and the United States, and finally throughout the world and were characterized in their early stages chiefly by conjunctivitis and impetigo. "Failure to recognize these commonplace and seemingly unimportant lesions as forerunners of disastrous epidemics in which serious complications have occurred has allowed epidemics to progress before control measures were established," he said. One particular strain, 80/81, is responsible for the majority of these epidemics in all parts of the world.

Dr. Chester W. Howe, associate professor of surgery, Boston University School of Medicine, said, "In terms of morbidity, prolongation of hospital stay, economy, necessity for further surgical risk, and particularly from the point of view of massive contamination of the hospital environment . . . postoperative staphylococcal infections are a particularly important problem in surgery." Although the pathways by which staphylococci gain access to a clean wound are not known, he reported suggestive evidence which indicates that the majority of such infections begin in the operating room. He urged extensive study of the problem and said, "There is no doubt that its significance is of such extent that it warrants the exp[illegible] amount of money and effort wh[illegible] be required."

Dr. David E. Rogers, associate professor of medicine, New York Hospital–Cornell Medical Center, New York City, stated, "In contrast to the experience of pediatric and surgical services, staphylococcal infections in non-operated adults on medical wards are nonepidemic, occur in a small number of patients, and have been relatively constant in incidence for a number of years."

Dr. Frederick H. Wentworth, medical director of disease control activities, Ohio Department of Health, Columbus, cited case histories indicating the seriousness of family infections resulting from patients carrying the disease home from the hospital. In one family, an infant was discharged from the hospital in October, 1954, and soon showed symptoms of a hospital-acquired impetigo. From then until July, 1958, there has never been a time when one or more of the five members of the family did not have some infection, and the cost of their care, exclusive of hospital bills, has been more than $1,500.

Dr. John E. Blair, bacteriologist, Hospital for Joint Diseases, New York City, pointed out that it is not practical for most hospitals to do their own phage typing of strains since it is hard to maintain the phages and requires highly trained personnel to do the typing. He advocated the use of regional laboratories as means of keeping better control over the quality of phages and of assuring the consistency of tests. He suggested that cultures be submitted only on a series of related sources, not on isolated cases.

Dr. John C. Colbeck, chief of service in the [illegible]ment, Shaughnessy Veterans Hos[illegible], British Columbia, Canada, suggested that small hospitals may afford especially good opportunities to study how infections spread. "In large hospitals, the possible routes of spread are so numerous that the probable method of spread is all too often indeterminable. . . . It might be wise for public authorities to consider the establishment of research units, with full laboratory facilities, in the smallest hospitals."

Dr. Dean A. Clark, general director, Massachusetts General Hospital, Boston, declared that hospital-acquired staphylococcic disease is always a community problem, never limited to the four walls of a particular hospital, since many, if not most, infections in patients become apparent only after discharge. He urged that hospital administrators plan to follow up at least a random sample of discharged patients and make suitable arrangements with their medical staffs, other hospitals in the area, and the health department to collaborate in such follow-up procedures in order to assure the detection of all related cases.

was associated with increased pressure in the renal veins, 2 had thrombosis of the renal vein, 1 had constrictive pericarditis, and 1 had tricuspid stenosis.

Treatment in the nephrotic syndrome should be directed toward the edema, to the underlying renal condition, and to specific etiological factors when these can be determined. At present treatment is largely of a nonspecific nature, although with increasing accuracy in diagnosis this will change. Salt restriction is designed to prevent edema and to initiate diuresis, and while low-salt diets are widely prescribed, little attention is paid by many clinicians to ensuring that these are sufficiently low in sodium. Limitation of salt intake is now relatively easy with low-sodium milk powders. In some patients with severe and prolonged proteinuria, deficiencies of both calcium and potassium may occur, with resulting bone rarefaction and hypokalemia. Both these defects are corrected by high-protein diets, with the use of low-sodium milk powder, although additional potassium may be required in the early stages of treatment. The value of steroid therapy in the nephrotic syndrome is still to be determined. Many have used ACTH or cortisone in short courses for from 10 to 15 days, with large doses simply as a "diuretic," and there is little doubt that many patients will show loss of weight and of edema with this treatment.

Fungus Disease in Northern California. L. A. Rantz, C. Halde, D. Newstrand and D. Kettner. California Med. 89:245-249 (Oct.) 1958 [San Francisco].

In an attempt to get information concerning the importance of fungi as cause of disease in northern California, the authors studied specimens from superficial lesions, such as hair, skin, and fingernails, obtained from 1,544 patients. Potential pathogenic fungi, particularly Microsporum audouini, Trichophyton rubrum, and T. tonsurans, were found in 542 specimens. These findings indicated that superficial mycotic infections were commonplace but that systemic illness caused by these organisms was uncommon.

The authors report on 1,449 patients from whom sputum, bronchial and gastric washings, pleural fluid, collections of pus, and other clinical materials were obtained and studied for systemic fungous infections in the department of medicine of Stanford University. Three hundred sixty-one of these patients were infected by Coccidioides immitis, Nocardia asteroides, Actinomyces bovis, or Cryptococcus neoformans. Most of these examinations were made routinely without reference as to whether or not the patient was thought to have a mycotic disease. Infection by these 4 kinds of fungus was proved in 8 patients in the whole group in whom disease caused by these organisms was considered possible. The incidence would have been greater if the source of the materials had been more carefully screened. In several of the 8 patients the clinical situation suggested mycotic disease. It is evident that the routine examination of a large number of clinical specimens does not uncover many instances of unsuspected systemic fungous infection. Candida organisms in large numbers were recovered from the sputum, from material obtained on nasopharyngeal and vaginal swabs, and from stools of a considerable number of patients, many of whom had received antimicrobial therapy. It was nearly always difficult to assess the role of these fungi in the causation of various manifestations of the patient's illness. In no case was pulmonary candidiasis definitely diagnosed, and in only 3 cases was there positive evidence of disseminated infection caused by these organisms. Candida organisms of various species are often recovered from clinical materials, but the role they play in the causation of disease is always difficult to ascertain. Serious infection by this group of organisms is most likely to occur in debilitated persons who have received antimicrobial therapy.

Lymphogranuloma Venereum: A Review of 61 Cases. D. Erskine. Brit. J. Ven. Dis. 34:163-165 (Sept.) 1958 [London].

This report is concerned with 61 male patients who were treated for lymphogranuloma venereum in the Seamen's Hospitals, London, between 1950 and 1957. With a few exceptions, they were admitted to hospital for treatment. Most of them presented in the venereal diseases department with a swelling in the groin; only a few were referred from the casualty department or from the surgeons, and consequently the author did not see the divers manifestations of this condition. In only 4 patients were transitory primary lesions detected. With one exception, all the patients were probably infected overseas, although not all gave a history of risk of infection, and they would often have passed the initial phase before presenting with a bubo. In some cases language difficulty, and in others the patient's lack of observation, may account for the absence of reported initial lesions.

The author suspects that some patients, in whom genital herpes, balanitis, and nonspecific urethritis were diagnosed at his clinic, may have later presented themselves with buboes at other clinics. He recalls one patient who reported with 3 tiny erosive ulcers in the coronal sulcus; there was no glandular enlargement, and a diagnosis of genital herpes was made, because routine investigations such as the Frei test were negative. The serologic complement-fixation test was reported positive to dilution 1:96 after the patient had left the clinic cured of his herpes a few days later. He returned 3 months later with a recurrence of the genital herpes, and now the inguinal nodes on the left were enlarged.

The Frei test was strongly positive, and the lymphogranuloma complement-fixation test was positive to dilution 1:144. It seems that a positive Frei test may be slower in developing than the serologic reaction, and one doubtful or negative test should not be considered final in the early stages of suspicious lesions. The incubation period of the bubo averaged 5 weeks.

Thirty-two of the 61 patients were treated with Terramycin, which the author considers to be the drug of choice—21 with two 10-day courses, separated by a 7-day interval (total 4 Gm.), and 11 with one course (20 Gm.). Nine patients were treated with sulfonamides alone, 6 with sulfonamides and Aureomycin, 7 with Aureomycin alone, and 7 with 3 courses of various combinations of sulfonamides and tetracyclines. The clinical response was satisfactory in 51 of the 61 cases. The significance of this clinical cure in relation to absolute cure is difficult to assess. The reversal of the serologic reaction was delayed, although, when it was possible to check the complement-fixation test a year or so later, reversal was found in the majority of patients in whom 2 or more courses of treatment had been given.

Anuria Complicating the Treatment of Leukemia.

R. A. Kritzler. Am. J. Med. 25:532-538 (Oct.) 1958 [New York].

Urinary suppression due to precipitation of urate in the urinary outflow tract occurs in leukemia more frequently, particularly after vigorous chemotherapy, than is generally appreciated, and presents a hazard that should not be ignored. The author reviews previously reported data on this problem and presents 3 new cases of which 1 was a case of acute leukemia. The first of the 3 new cases concerned a 65-year-old woman, in whom anuria and uremia were due to blockage of the ureters and renal pelves by urates excreted in increased amounts, presumably as a consequence of treatment with radioactive phosphorus. Fluid intake at the time of treatment was not sufficient. A diuresis followed pyelostomy. The precise cause of death was not clear.

The second case concerned a 63-year-old man, in whom anuria and moderately severe uremia occurred during the 10th week of a gradual fall in leukocytes while chlorambucil was given. Diuresis and recovery followed ureteronephrostomy and removal of urate precipitate on one side. Leukemic or nonleukemic renal failure seems excluded by the fact that prior to the anuria the patient received a course of triethylene melamine without renal complications, and later, when a course of chlorambucil was repeated with adequate fluid intake, there was no oliguria, crystalluria, or significant rise in the blood urea nitrogen level. The anuria is considered to have been a complication of therapy, probably precipitated by dehydration due to hot weather.

The third patient was a 41-year-old woman, in whom a number of factors contributed to the development of acute anuria. At the time treatment was begun there had been high fever and vomiting. The pretreatment serum nonprotein nitrogen elevation was probably due in part to dehydration and in part to renal insufficiency associated with leukemic infiltration of the kidney. The recorded fluid intake during the first days of cortisone treatment appeared inadequate. The fall of circulatory leukocytes from a high level was extraordinarily precipitous. The blood uric acid level reached 35 mg. per 100 cc.

Data on the 3 cases described and on the 7 previously reported are tabulated. All but 2 of the patients were over 50 years of age. Nine of the 10 patients had chronic leukemia (6 myeloid, 3 lymphatic). In all instances the number of circulating leukocytes was high before treatment was begun and was considerably lower at the onset of anuria. The interval from the beginning of treatment to the development of oliguria was short (2 or 3 days) in some cases and long (62 days) in others. The mortality from this complication was high; only 2 patients survived.

The author feels that the following factors are contributory to the development of this rare complication: (1) age, the 5th and 6th decades; (2) high urinary output of urate and tendency to calculus formation in the untreated patient with leukemia; (3) further increase in urinary urate excretion due to destruction of large numbers of leukocytes or to inhibition of the formation of leukocytes and associated incorporation of purines by the therapeutic agent; and (4) dehydration and inadequate volume of urine. It is advisable to recommend a high fluid intake to all patients with leukemia during the first few weeks of any kind of therapy directed toward reduction of the mass of leukemic cells.

Frequency and Classification of Glucosuria in Older Hospital Patients without Marked Symptoms of Diabetes: Frequency of Diabetes in Medical Department.

J. Pedersen and N. I. Nissen. Ugesk. læger 120:1319-1323 (Oct. 2) 1958 (In Danish) [Copenhagen].

In 10% of 260 afebrile patients, aged over 50 years, without recognized diabetes or glucosuria, whose first nocturnal specimen of urine did not give positive reaction with Fehling's solution, routine examination of an average of 4 24-hour specimens of urine with Tes-Tape in the course of the first 2 weeks of hospitalization revealed spontaneous glucosuria twice as often in men as in women. The amount of glucose determined quantatively by the ferric cyanide method was minimal and intermittent. None of the patients showed glucosuria in all specimens, and half of them had glucosuria in only 1 out of 4 24-hour specimens. About 3% of all the patients had diabetes, about 3% were observed for diabetes, and about 4% had nondiabetic glucosuria. Comparison of the last-named group with a nondiabetic aglucosuria control group showed identical average fasting and 24-hour blood sugar levels and glucose tolerance curves, which is regarded as proof that this glucosuria group is nondiabetic. Comparison of the group of diabetic patients with intermittent glucosuria with an equal-numbered group of patients with diabetes without glucosuria showed higher fasting blood sugar and broader glucose tolerance curves and, on the average, higher clinical renal threshold in the second group. Partial diabetes in older patients is hard to diagnose, largely because the glucosuria is intermittent. The glucose-oxidase method does not exclude diabetes in spite of repeated negative reactions. The method must be combined with examinations of the blood sugar in suspected diabetic patients whose urine gives negative Tes-Tape reaction.

SURGERY

Carcinoma of the Head of the Pancreas: A Study of 21 Cases. R. B. Eaton. Canad. J. Surg. 2:15-21 (Oct.) 1958 [Toronto].

Eaton shows that a renewed interest has developed in the treatment of carcinoma of the head of the pancreas and ampulla of Vater, since Whipple and associates in 1935 demonstrated the feasibility of pancreatoduodenectomy. Reviewing several series of cases reported in the literature, he finds that, although the operative mortality rate has been reasonable, survival in carcinoma of the head of the pancreas has been of short duration. On the other hand, lesions limited to, or originating from, the ampulla of Vater or duodenal mucosa present a brighter picture, and quite a number of 5-year cures have been reported. It seems that there is an unwarranted delay in the diagnosis and management of many of these cases before surgery is contemplated. Twenty-one patients with carcinoma of the pancreas were observed by the author in his own private practice during the last 6 years; 8 patients were found suitable for pancreatoduodenectomy, 8 had palliative operations, and 5 were considered beyond operative relief.

Pain was usually the first complaint, and it gradually increased in intensity. It varied in type from a mild colicky or spasmodic pain to a boring sensation; it was usually located in the mid-epigastrium or the hypochondriac region on the right. Occasionally, it was aggravated by the taking of food. Jaundice was the presenting symptom or sign in all but one patient, although in most patients it was not the initial symptom. Associated with these 2 main symptoms were anorexia, nausea and vomiting, fatigue, constipation, and loss of weight. The liver was enlarged in most patients. A tumor was palpable only in a few advanced cases. Preoperative therapy consisted of the administration of vitamins K, B, and C and glucose solutions and blood transfusions.

In 3 of the 8 patients subjected to pancreatoduodenectomy, an end-to-end (Billroth I type) gastrojejunostomy was carried out, the pancreatic stump being implanted end-to-side into the jejunum just beyond this anastomosis. The common bile duct likewise was implanted into the jejunum some distance beyond the latter anastomosis, and a side-to-side enteroenterostomy was made opposite the site of implantation of the pancreas. In the other 5 patients the open end of the jejunum was closed, and the common bile duct, the pancreatic stump, and the stomach were implanted (in that order from above downwards) end-to-side into the jejunum. The second method was found to be preferable, chiefly because it appeared to fit into the reconstruction more easily and reduced operation time by eliminating the enteroanastomosis. There were few digestive complaints after either method. One patient died as a result of the operation. Of the 7 patients who survived pancreatoduodenectomy, all remained alive and well for more than a year, 1 patient being still alive 30 months after operation and enjoying good health. The average survival in the 8 patients undergoing the palliative procedure was less than 6 months. Pancreatoduodenectomy is a justifiable procedure in many patients with carcinoma of the head of the pancreas.

Closed Surgery in Atrial Septal Defect: Report on 70 Cases. H. G. Davidsen. Acta chir. scandinav. 115:343-361 (No. 5) 1958 (In English) [Stockholm].

The author reports on 26 male and 48 female patients, between the ages of 4 and 47 years, with atrial septal defects who were admitted to the department of surgery of Rigshospitalet in Copenhagen. The functional capacity of the patients was recorded preoperatively and postoperatively, and the patients were grouped in 4 functional classes according to the criteria laid down by the New York Heart Association in 1953. Two of the 74 patients died on the operating table before the correction of the defect. Surgical intervention was limited to an explorative atriotomy in 5 patients. Closed operative techniques were employed in the remaining 67 patients; the semicircular suture method was used in 15 of the patients, the circumclusion suture technique was used in 40, and atrioseptopexy was performed on 12. Six anatomic types of atrial septal defect were observed at the surgical intervention: (1) superior marginal defect; (2) central defect; (3) multifenestrated membranous interatrial septum; (4) simple primum defect; (5) primum intermedium defect; and (6) persistent *ostium atrioventriculare commune.*

The results of the operative treatment were determined by measurement of the intracardiac shunts and by the changes in the cardiac murmurs and the heart volume. It was found that, if the murmurs had disappeared completely, or if the volume of the heart had been reduced to less than 75% of the preoperative volume, the shunt had been eliminated. The semicircular suture technique failed because the sutures pulled through the myocardial fibers; this technique was abandoned on account of the unsatisfactory results. Atrioseptopexy proved particularly valuable in patients with a superior marginal defect in whom both the defect and the accompanying anomalous drainage of the right pulmonary veins may easily be corrected. Circumclusion suture gave good results in patients with central defects and multifenestrated membranous septum, and fair results in those with simple primum defect. Difficulties, however, were met even in patients with central defects if these were located too close to the opening of the inferior vena cava. None of the techniques used were effective in patients with primum intermedium defect and with persistent ostium atrioventriculare commune. Open methods which make possible repair under direct vision are regarded as the only chance for surgical treatment in these cases, although even these methods may often fail because of the frequent presence of severe valvular malformations in patients with these types of defect.

The most important operative complications associated with the closed surgical methods are those interfering with the valvular function or the drainage of the pulmonary veins. An abnormally large valve of the inferior vena cava (valvula eustachi) may be the cause of impaired drainage of the inferior vena cava. A persistent septum spurium may conceal the anatomic conditions in patients with a superior marginal defect. The circumclusion suture may cause thrombosis if a part of the suture material is left uncovered by the septal endothelium, and in 5 of 7 cases this condition did not cause any untoward reactions. Anomalies of the cardiac rhythm were uncommon except in patients operated on with the aid of hypothermia. Some postoperative complications could probably be considered as specific for the operative techniques. Nodal rhythm or atrioventricular block occurred in some patients after circumclusion suture, but disappeared again later. Transitory paresis of the right phrenic nerve was observed not infrequently until a new operative practice was introduced by which the pericardium was opened at a good distance anterior to the phrenic nerve. The operative techniques employed did not differ significantly with regard to complications and mortality rate. In addition to the 2 patients who died on the operative table before the correction of the defect, 5 died postoperatively, including 1 who died 10 months after the operation. Six of the 7 deaths occurred in patients with pulmonary artery hypertension and 5 in patients in the functional classes 3 and 4. None of the patients having normal pressures and being grouped in functional class 1 or 2 died.

Hypophysectomy in Disseminated Cancer of the Breast. E. Andersson. Acta endocrinol. 29:295-301 (Oct.) 1958 (In English) [Copenhagen].

Hypophysectomy was performed at the neurosurgical department of the University Hospital in Copenhagen on 50 women, between the ages of 39 and 72 years, with advanced cancer of the breast of from 1 to 6 years' duration, with diffuse metastases to bones and soft tissues, in whom all other methods of treatment such as irradiation and hormone therapy had failed. Immediately before the hypophysectomy the patients were given 200 mg. of cortisone by intramuscular route. In the operating room the patients were given 100 mg. of hydrocortisone dissolved in 500 cc. of dextrose solution as an intravenous drip. Immediately after the operation the patient received another intramuscular injection of 200 mg. of cortisone, and cortisone was given twice daily for the first 5 postoperative days in doses of 150, 100, 75, 50, and 25 mg. respectively. Maintenance treatment consisted of 25 mg. of cortisone given twice daily, and 100 units of thyroid extract were administered daily. The postoperative course on this regimen was smooth in most patients. There was a postoperative increase in the urinary output which resulted from the removal of the posterior lobe of the hypophysis in addition to that of the anterior lobe.

Hypophysectomy was tolerated well; only 3 patients died within the first 2 weeks. It produced a remission in 21 of the 50 patients operated on, with relief of pain and restoration of the temperature and blood to normal. Metastases remained stationary in 16 of the 21 patients, and regressed in 5. The average duration of the remission was about 8 months. The most favorable effects of hypophysectomy were obtained in menopausal patients. Patients with metastases to the liver and brain did not respond. Blindness in the right eye occurred in 6 patients in whom the optic nerve had to be cut because of technical difficulties in the course of the operation. Seventeen patients stated that they had lost the sense of smell after the operation. The reported data show that hypophysectomy can produce a remission of varying duration in otherwise hopeless cases of breast cancer with widespread metastases. There may be subjective improvement, relief of pain, and a considerably decreased consumption of analgesics in some of the patients without remission. Hypophysectomy marks an advance in the treatment of patients with far-advanced breast cancer.

Arterial Catheterization Used for Pressure Measurement from the Left Ventricle in Patients with Chronic Constrictive Pericarditis. A. Actis Dato and F. Morino. Minerva med. 49:3296-3306 (Sept. 1) 1958 (In Italian) [Turin, Italy].

Intraventricular hemodynamic pressure in the left ventricle was measured by catheterizing the humeral artery in 10 patients with chronic constrictive pericarditis. Intraventricular hemodynamic pressure in the right heart was also recorded in 8 of these patients. The clinical findings showed that pericardial constriction, affecting in an equal degree the right and the left heart, was present in 3 patients, that a more severe constriction of the left than of the right heart was present in 5, that right ventricular insufficiency existed in 1, and that a mild form of pericardial constriction was present in 1. These findings were confirmed by intraventricular hemodynamic pressures measured by the cardiac catheterization technique. Ventricular fibrillation developed in 2 patients during the catheterization procedure. After a short pause, catheterization was resumed and completed without further disturbance.

This investigation justified the following conclusions: Cardiac catheterization is a useful means of examining congestion of either the right or the left ventricle. It can reveal on which side of the heart the pericardial constriction is more severe, and it can show that there is a correlation between the intraventricular hemodynamic pressure tracings from both ventricles and the clinical picture. Consequently, the intraventricular hemodynamic pressure tracings from both ventricles can be used as a guide to determine which side of the heart should be more exposed to surgical therapy. The authors suggest that arterial catheterization used for pressure measurement of the left ventricle should not be routinely used in patients with chronic constrictive pericarditis. It can be used only after the clinical examination, roentgenologic and angiocardiographic findings, and catheterization of the right heart have failed to formulate a clear picture of constrictive pericarditis, this being a necessary condition for instituting an effective surgical therapy.

Protrusion of Lumbar Disks Causing Marked Bilateral Weakness of the Legs. H. E. Storino, R. E. Siekert and C. S. MacCarty. Minnesota Med. 41: 687-690 (Oct.) 1958 [St. Paul].

Protruded or extruded lumbar intervertebral disks may so compress the cauda equina that the patient is rendered paraplegic with sphincteric disturbances and saddle anesthesia. A review of the records of 4,330 patients, who had undergone laminectomy at the Mayo Clinic for protrusion of a lumbar disk during the past 5 years, revealed 21 patients who had reduction in motor power in their lower extremities of 50% or more. These form the basis of this report. Less than 0.5% of patients operated on for protruded lumbar disks in the period under consideration had marked weakness of the lower limbs. Patients with slight weakness in one or both lower limbs were frequently encountered but were not included in this study. In the majority (19 patients) the onset of the episode which led to operation was well delineated, with the first symptom being sudden pain in the lower part of the back with or without concomitant pain in the lower limbs. The pain varied from mild to severe. After several days or a few weeks almost all these patients had unilateral or bilateral sciatica.

Although in a few patients the weakness developed within hours, in most the onset of muscular weakness was gradual over a period of 1 or 2 weeks. Furthermore, something usually seemed to precipitate or aggravate the weakness. Such acts as expelling an enema, sneezing in the bent-over position, gagging while brushing the teeth, or trauma in the form of strenuous muscular effort, such as lifting a heavy object, manipulative therapy, and leg traction, initiated the attack or converted a relatively mild one into one with marked muscular weakness. No correlation was found between the level of the disk involved and the distribution of pain. The pain, however, tended to decrease as the weakness appeared and increased. Sensory disturbances were noted in 18 patients and difficulty with the urinary bladder in 11; 10 of these 11 also had difficulty with the anal sphincter. Return of function after operation was excellent in 5 patients and good to fair in 7 of the 15 for whom adequate follow-up was available. In 3 patients no return of function occurred. Early diagnosis and operation are important in obtaining a successful result.

Homeoplastic and Alloplastic Transplantations of Aorta. K. Kremer and H. W. Heupel. Chirurg 29:448-453 (Oct.) 1958 (In German) [Berlin].

Eight male and 5 female patients, between the ages of 11 and 38 years, were operated on at the surgical clinic in Düsseldorf, Germany, for aneurysm of the thoracic aorta, extensive stenosis of the aortic isthmus, and severe degenerative changes in the wall associated with stenosis of the isthmus. A homeoplastic graft, 4 to 8 cm. in length, was used in 8 patients, and a cylindrical Ivalon sponge transplant, 4.5 to 7 cm. in length, was employed in 5. One of the 8 patients with free transplantation of homeoplastic aortic graft died of obstructive thrombosis which originated from an aneurysmatically dilated intercostal artery located distal to the graft. The 5 patients in whom Ivalon sponge grafts were used were followed for periods up to one year, and the clinical results were highly satisfactory. Healing over of the grafts occurred without complications, such as effusion or allergy. The material seems to exert a specific plastic effect which leads to a rapid and close union within the suture area. The Ivalon sponge grafts have many advantages over the homeoplastic grafts: they are more easily available; they can be manufactured in any number, size, and form; they can be sterilized simply and safely and can be stored without any special care. No degenerative changes in the sense of atheromatosis or calcification have to be reckoned with when Ivalon sponge grafts are used. By the recent use of contrast-providing threads it has become possible to show the wall of the graft in the roentgenogram and hence to follow the outline of the graft in the roentgenogram and to prevent occasional complications by aneurysmatic dilatations. Careful control for additional years will, however, be required to obtain definite proof of the superiority of the Ivalon sponge grafts over the homeoplastic grafts.

Hazards Attending the Use of Esophageal Tamponade. H. O. Conn. New England J. Med. 259: 701-707 (Oct. 9) 1958 [Boston].

Experience with the Sengstaken-Blakemore tube at the Grace-New Haven (Conn.) Community Hospital suggested that complications during the use of esophageal tamponade are more frequent, more varied, and more serious than generally recognized. The Sengstaken-Blakemore tube was employed on 81 occasions in 50 patients with esophageal varices who were hospitalized from 1950 to 1957 at this hospital. The nasogastric tube was usually passed according to the directions supplied by the manufacturer. The gastric balloon was ordinarily inflated with 100 to 250 ml. of air; the pressure maintained in the esophageal balloon ranged from 20 to 40 mm. Hg. The average period of intubation was 78 hours, ranging from 10 minutes to 12 days. The total duration of intubation per patient was 121 hours, ranging from 30 minutes to 30 days. In 19 of these patients major complications developed during esophageal tamponade; 9 of them died as a direct consequence of these complications. In 6 additional patients factors complicating esophageal tamponade contributed directly to the fatal outcome; rupture of the esophagus occurred in 1 of these. Potentially fatal abnormalities in the use of esophageal tamponade occurred during 55 of the 81 episodes. Obstruction of the airway, which was caused either by regurgitation and bronchial aspiration of bloody gastric secretion or by the displaced esophageal balloon, was the most serious complication. In addition to major complications, such as 2 deep erosions in the proximal portion of the esophagus just below the arytenoid cartilage, there were minor complications which led directly or indirectly to a fatal result. Only 10 patients were entirely free of these difficulties during esophageal tamponade. Forty-one of the 50 patients died.

Considering these fatal complications, the question arises: Should this form of therapy be abandoned? Despite these disturbing statistics, esophageal tamponade still plays an important part in the treatment of patients with bleeding esophageal varices, especially those unable to tolerate surgical intervention. Bleeding seemed to be controlled, at least transiently, by this treatment in approximately 70% of the patients. In view of the high mortality among patients with hemorrhages of esophageal varices, regardless of the type of therapy employed, it is reasonable to assume that many patients of this series who died of complications of esophageal tamponade would have died of other causes.

To prevent the most serious hazards of this therapy, more emphasis should be placed on a better understanding of the apparatus and on more careful observation of the patient. A new tube should be used for each treatment, and the gastric contents aspirated immediatly after intubation. Constant, or frequent, intermittent gastric suction should be performed to empty the stomach and to evaluate control of the bleeding. Nothing should be administered orally. When esophageal tamponade is being used, one error of technique or judgment or a single unlucky accident may be enough to set in motion a series of events leading to death. It behooves those who employ this apparatus to know it intimately, to use it carefully, to avoid predictable pitfalls, and to anticipate unpredictable complications.

Pulmonary Resections for Metastatic Lesions. J. L. Ehrenhaft, M. S. Lawrence and D. M. Sensenig. A. M. A. Arch. Surg. 77:606-612 (Oct.) 1958 [Chicago].

The results of surgical treatment of proved metastatic pulmonary malignancy at the University Hospitals, State University of Iowa, Iowa City, are given. Fifty-five carefully selected patients underwent exploratory thoracotomy. Pulmonary resections were carried out in 37 of these patients. In the group of 28 patients who had resections for carcinoma, 3 are alive from 2 to 7 years postoperatively. Of 15 patients undergoing exploration but without resection, 3 are alive from 1 to 2 years after the operation. In the group of 9 patients who had resections for sarcoma, 1 patient is alive 5 years and 2 patients are alive 2 years after the operation. The 3 patients with metastatic sarcoma who had exploration but not resection died within 4 months. The number of patients involved is small, but the figures do not give the impression that the results are better among the patients with metastatic sarcoma than among those with metastatic carcinoma, as found in data from another study. No indication that salvage of the patient is related to the type of pulmonary resection was found. In this series there is no correlation of the length of time between treatment of the primary lesion and the appearance of pulmonary metastatic disease with salvage of the patient. A long interval is not necessarily associated with an increased survival rate. The type of tumor and its biological behavior are probably the most important factors. The results of surgical treatment of metastatic pulmonary breast cancer have been so discouraging that it appears that pulmonary resection is not justified. Yet when distressing pulmonary symptoms can be relieved, operation seems justified, even though prolonged survival after removal of pulmonary metastatic neoplasms may not be obtained. This complex problem needs periodic reporting of results. Pulmonary resection for metastatic lesions is indicated in carefully selected patients, as a small percentage of them will be cured of their disease and others will receive palliation of distressing symptoms.

OPHTHALMOLOGY

Glaucoma Following Radiotherapy. R. F. Jones. Brit. J. Ophth. 42:636-638 (Oct.) 1958 [London].

The author reviews previously reported cases of glaucoma after radiotherapy and presents another case. The patient was a 40-year-old woman, who complained of nasal obstruction on the right side. A large polyp was removed, which proved to be a mucoid adenocarcinoma. Between December, 1954, and January, 1955, the area was treated by radiotherapy. Later a right-sided Caldwell-Luc operation with removal of the right middle turbinate bone was undertaken, and, as a recurrence of the carcinoma was found in the middle turbinate, a partial posterior fenestration of the right side of the palate was performed with intercavity irradiation by radium.

The patient noted that the right eye was dry and the vision blurred in April, 1956, and sought an opinion on May 7, after 3 weeks of visual disturbance. The ocular tension (Schiötz) was 32 mm. Hg in the right eye and 27 mm. Hg in the left. Gonioscopy showed the angles to be of medium width. In the right eye newly formed tortuous blood vessels occupied the angle and overlaid the peripheral iris. On June 11, the ocular tension had reached 45 mm. Hg. A week later the visual acuity had deteriorated, and corneal edema was present. The ocular tension was then 50 mm. Hg, and the fundus remained hidden after that date. The patient was now in pain, and cyclodiathermy was performed on June 21. After this, ciliary injection, corneal edema, and an anterior chamber flare developed, and the ocular tension remained between 42 and 45 mm. Hg (Schiötz), although pilocarpine and Diamox were administered. Later cyclodiathermy was repeated, the patient became free of pain, and the tension fell to 22 mm. Hg. The visual acuity was now the ability to count fingers.

Theoretically, the radiotherapy could have disturbed the inflow-outflow balance by producing an occlusion in the anterior ciliary veins, in the vortex veins, or in the central retinal vein. However, the finding of dilated, tortuous, varicose, newly formed vessels in the iris and angle after radiotherapy may be considered the causative factor in the onset of glaucoma.

THERAPEUTICS

Acute Meprobamate Poisoning. L. W. Powell Jr., G. T. Mann and S. Kaye. New England J. Med. 259:716-718 (Oct. 9) 1958 [Boston].

A review of the literature revealed 11 cases of attempted suicide with large quantities of meprobamate. The patients took amounts ranging from 10 to 40 Gm. of this drug, and all recovered. The symptoms varied from sleepiness through stupor and coma to complete respiratory and circulatory collapse. Coma, areflexia, and lowered blood pressure occurred in most patients. The pulse became rapid in most, but was slowed to 40 per minute in one. One patient was cyanotic, and another had slightly cyanotic lips. Four patients had pinpoint pupils, and 2 had dilated, fixed pupils. Treatment was in accordance with the symptoms. Gastric lavage occasionally recovered a considerable part of the ingested drug, and an oral airway was inserted in several patients to insure unobstructed respiration. Tracheal aspiration relieved respiratory embarrassment in one patient. A variety of central nervous system stimulants were used, such as dextro amphetamine sulfate, amphetamine sulfate, caffeine and sodium benzoate, pentylenetetrazol, picrotoxin, and coffee. The prognosis was generally good regardless of which analeptics were used. Meprobamate poisoning is often associated with hypotension which has been treated with intravenous infusions and vasopressor substances, such as phenylephrine and levarterenol bitartrate. Overhydration, however, should be avoided in these patients because of their flaccid state.

The autopsy findings for 2 women who succeeded in committing suicide by taking 12 and 20 Gm. of meprobamate are interesting, because they are apparently the first cases of death resulting from this tranquilizing drug. One woman weighed 110 lb. (50 kg.), and the other weighed 125 lb. (57 kg.). In the first woman 12 Gm. of meprobamate would represent a dose of 240 mg. per kilogram of body weight, and in the second woman 20 Gm. would represent 350 mg. per kilogram of body weight, both of which are below the lethal dose in animals.

The fact that other persons have survived the ingestion of much larger amounts of meprobamate suggests that early symptomatic treatment may sometimes be lifesaving in certain cases, although there may be individual variation in susceptibility to the acute toxic effects of the drug.

A New Depot Penicillin: Bipenicillinate of Diphenylpiperazine. H. Beerens and V. Macquet. Presse méd. 66:1418-1419 (Sept. 17) 1958 (In French) [Paris].

Bipenicillinate of diphenylpiperazine (BPDP) (2,5-diphenylpiperazine bis-benzylpenicillin G) is a new penicillin salt composed of 2 molecules of penicillin G joined by a diphenylpiperazine link—a comparatively simple link free from toxicity. The new product is slow to dissolve in water or serum, and this probably explains its prolonged action. It has an antibiotic activity of 1,310 units per milligram. Experiments showing that the drug was well tolerated and that it produced high concentrations in the blood were soon followed by clinical trials in which equally good results were reported. The findings so obtained have been confirmed by the present study in which the authors investigated the levels of penicillemia found in patients after the intramuscular administration of BPDP, procaine penicillin, and Bipenicillin (a mixture of 600,000 units of procaine penicillin and 400,000 units of penicillin G).

Comparison of the 3 sets of figures obtained showed that, while the blood levels produced by each of these forms of penicillin were identical 3 hours after administration, the subsequent rate of decline was lowest for BPDP, so that 9 hours after administration the levels produced by this drug were higher than those produced by the other 2. The injection of one million units of BPDP produced blood levels of more than 1 unit per milliliter in 15 minutes, and a maximum concentration of more than 3 units per milliliter in one hour. The prolonged action of the new penicillin was shown by the fact that effective therapeutic concentrations were still present 12 and 24 hours after injection. Tolerance for BPDP was perfect; the intramuscular injections were painless, and none of the patients suffered any cutaneous or anaphylactic reactions.

A Clinical and Laboratory Comparison of the Effects of Commonly Used Vasodilator Drugs on Arterial Diseases. J. M. Stallworth, W. H. Lee, C. Belisle and D. B. Nunn. Am. Surgeon 24:700-708 (Oct.) 1958 [Baltimore].

Arlidin, Ilidar, Priscoline, and Drug 5029 were used in this investigation. Nylidrin (Arlidin) hydrochloride is a synthetic compound belonging to the epinephrine-ephedrine group. Its primary sympathomimetic actions are to dilate the small vessels in skeletal muscle and to increase cardiac output. Azapetine (Ilidar) hydrochloride is a dibenzasepine adrenergic blocking drug. It has been described as being adrenolytic and sympatholytic, having direct vasodilating effect on arteries and having an epinephrine reversal property. Tolazoline (Priscoline) hydrochloride is related to both sympathomimetic amines and histamines. This drug is reported to act synergistically with epinephrine on the animal heart and to increase cardiac output. In addition, it supposedly is an adrenolytic and sympatholytic agent. Phenoxyisopropylnorsuprifen (Drug 5029) is a European product. Reports on this drug indicate that its properties and structure resemble those of nylidrin hydrochloride.

Fifteen patients with peripheral vascular diseases underwent detailed laboratory studies before, during, and after infusions of the 4 vasodilators. None of the drugs showed consistently good results in all types of vascular diseases. The responses varied not only between persons with similar diseases but also from one extremity to another in the same person. Ilidar and Priscoline proved most effective in the majority of patients, especially as indicated by the detailed plethysmographic and temperature studies. There is excellent correlation between the effects of these drugs on the conjunctival vessels and the small vessels in the extremities, vessels that are easily accessible to photography in the testing of vasodilator drugs.

Vasodilator drugs that increase cardiac output must be administered with great caution in patients with heart disease. Additional studies on laboratory animals are indicated with regard to the effects of these drugs on the cardiac contractile force. It is postulated that each major system of arteries has its own "chemoreceptor mechanism," causing tremendous variations in the effects of vasoreactive drugs in different parts of the body at the same time.

Penicillin Treatment as Cause of Difficulties in the Diagnosis of Neurosyphilis. M. C. Mackenzie-Van Der Noordaa and F. M. Haagsma. Nederl. tijdschr. geneesk. 102:1595-1597 (Aug. 16) 1958 (In Dutch) [Amsterdam].

When patients with neurosyphilis are treated with penicillin, the typical signs of dementia paralytica may disappear from the cerebrospinal fluid within a year, despite the fact that the patient's condition becomes progressively worse and the diagnosis of dementia paralytica has been confirmed. The authors observed this in 4 patients. If a patient has the clinical symptoms of dementia paralytica, although the spinal fluid does not show the characteristic changes, it should be borne in mind that a recent course of penicillin treatment may have masked the spinal fluid signs. Neurosyphilis is most likely to develop in patients who received inadequate or no treatment for their primary syphilitic infection. Therefore, penicillin should never be given to patients who happen to have a positive Wassermann reaction, unless the spinal fluid has first been tested for evidence of neurosyphilitic changes.

Clinical Experience with Warfarin Sodium. M. Toohey. Brit. M. J. 2:892-893 (Oct. 11) 1958 [London].

Warfarin sodium is a unique coumarin compound in that it can be given intravenously as well as by mouth. It has been stated that warfarin sodium is the "anticoagulant of choice." This paper describes observations on its use in 175 patients, most of whom had cardiovascular disease (myocardial infarction or cardiac failure) and the remainder had phlebothrombosis and pulmonary embolism. Treatment was controlled by the simultaneous use of Quick's and Owren's methods. A therapeutic level of between 2 and 3 times the normal control time (ideally 2½ times) was maintained when assessing results by Quick's method. For Owren's technique a level of between 10 and 14% was aimed at. Warfarin sodium was found to be a rapidly acting drug in that 95% of all patients reached a therapeutic prothrombin time in 36 hours. With daily doses of the drug just sufficient to maintain a therapeutic prothrombin time, the duration of action is approximately 36 hours. In large doses warfarin sodium has a sustained effect of up to 4 or 5 days. Therefore, large doses should be avoided. The usually recommended initial dose of 60 to 75 mg. proved far too much in this series; 35-to-50-mg. doses proved perfectly adequate for initial therapy, and it is inadvisable to exceed 50 mg. as an initial dose. The over-all average maintenance dose was 9 mg., and 80% of all patients were maintained on daily doses of between 5 and 15 mg.

Warfarin sodium proved extremely easy to control, and it probably ranks with phenindione as one of the 2 best anticoagulant drugs available for short-term therapy. Initial experience with warfarin sodium shows that it is also a useful anticoagulant for long-term therapy. In prescribing the anticoagulant, great care must be taken to allow for its cumulative effect. In this respect warfarin sodium resembles phenylpropyl-hydroxycoumarin, which has proved a reliable anticoagulant for long-term therapy. To obtain the best results with warfarin sodium, it is necessary to have available a strength of tablet with which to prescribe variations in dose of 0.5 mg. Scored 3-mg. and 5-mg. tablets would be ideal.

Clinical Evaluation of "Miradon." G. Kellaway. Brit. M. J. 2:889-891 (Oct. 11) 1958 [London].

Since the introduction of bishydroxycoumarin (Dicumarol) a number of hydroxycoumarin and indanedione derivatives, causing depression of the prothrombin activity of blood, have become available for use as anticoagulants. They all suffer the disadvantage of being potentially dangerous and require frequent estimations of the prothrombin time for their control. The new anticoagulant, anisindione (Miradon), appears to be more rapidly effective than, and just as readily controlled as, any anticoagulant in current use. In previous tests on animals Miradon had given no evidence of toxicity. This report is concerned with its therapeutic use in 25 patients requiring anticoagulant therapy.

The initial response to a loading dose of 300 mg. was rapid, and some effect upon prothrombin time was evident in most subjects in 6 hours. More than 50% of the patients had prothrombin levels within the desired therapeutic limits (prothrombin activity of 10 to 20%) at 24 hours, and 86% of subsequent estimations of the prothrombin time were within similar limits. Normal prothrombin levels were recorded between 36 and 72 hours after cessation of treatment, and an even response was evident during therapy. Vitamin K_1 produced a rapid reversal of anticoagulant action. Compared with other anticoagulants, Miradon appears to approach more closely to the "ideal" for a short-term anticoagulant than any at present in common use. The uniformity of response to a single daily dose suggests that it would prove satisfactorily also in long-term therapy.

Contribution to Problem of Failure of Oral Therapy in Patients with Diabetes Mellitus. S. E. Strauzenberg, H. Haller and H. Meyer. München. med. Wchnschr. 100:1535-1540 (Oct. 3) 1958 [Munich, Germany].

The authors report on 1,000 patients with diabetes mellitus who were treated with orally administered sulfonylurea compounds. From the beginning of their administration these drugs did not exert any effect on the carbohydrate metabolism of 202 (20.3%) of the 1,000 patients, who therefore were considered as primary failures. Twelve patients (1.2%) responded to the drugs for a short period ranging from 2 to 4 weeks, and after that the sulfonylurea compounds became rapidly ineffective; these patients were considered secondary failures. Seven hundred eighty-six patients were satisfactorily controlled by the sulfonylurea compounds for periods ranging from 6 to 8 weeks and also for much longer periods. The drugs then became ineffective in 33 (4.2%) of these 786 patients who were considered as genuine late failures. Not a single case of recent diabetes mellitus was observed among these 33 patients; the shortest duration of the disease was 2 years and the longest, 33 years.

No relationship was observed between age and body type of the patient and the incidence of late failure to respond to the sulfonylurea compounds. There was, however, a definite relationship between the incidence of such late failures and the quality of the control of the carbohydrate metabolism by the sulfonylurea compounds. Of 448 patients who were easily and satisfactorily controlled with the aid of these drugs, 0.6% were late therapeutic failures, as compared with 7% of 280 patients who had shown only a moderate response to the drugs (with an abnormal daily amount of 10 to 20 Gm. of sugar in the urine) and 13% of 120 patients who had been unsatisfactorily controlled with the aid of these drugs (the abnormal daily amount of sugar in the urine varying from 20 to 30 Gm.). In this last group complete failure of response to the sulfonylurea compounds occurred most rapidly. These findings strongly suggest that prolonged therapy with sulfonylurea compounds should be limited to patients with the most favorable response to these drugs.

Late failure to respond to the sulfonylurea compounds is to be considered as a manifestation of the progressive course of the disturbance of metabolism, such as may be observed with similar frequency in other patients who had not been treated with sulfonylurea compounds. The fact that the metabolism can no longer be controlled with the aid of the sulfonylurea compounds is explained by the authors' concept of the mechanism of action of these drugs. According to this concept, the sulfonylurea compounds no longer exert an effect on the carbohydrate metabolism when the production of insulin in the patient's body is cut off to such a degree that a certain required amount of insulin is no longer available. The authors do not share the opinion of other workers that exhaustion of beta-cell activity may be caused by the sulfonylurea compounds.

Two Years' Experience with Viomycin Pantothenate Sulfate (Vionactan) in Treatment of Pulmonary Tuberculosis. G. F. Scalfi, P. Pontiggia and G. Rossa. Minerva med. 49:3343-3356 (Sept. 5) 1958 (In Italian) [Turin, Italy].

An Italian preparation, viomycin pantothenate sulfate (Vionactan), alone or in combination with other antibiotics, was administered to 48 male patients, between 19 and 49 years of age, with pulmonary tuberculosis for a period of 2 to 6 months. Vionactan was administered in a daily dosage of 2 Gm. every 2 or 3 days to 8 patients with chronic disease, who had been previously receiving other antibiotics for at least 2 years. Vionactan and isoniazid in a daily dosage of 5 mg. per kilogram of body weight were administered to the patients at the same time after it had been proved that the tolerance of the patients to Vionactan was good. Vionactan alone was given to another group of 13 patients. The daily dosage consisted of 1 or 2 Gm. of the drug given every other day for a period of 3 to 5 months. The early phases of pulmonary tuberculosis were present in 4 patients. Vionactan brought about radical improvement in 2 patients and marked improvement in 2. [By "radical improvement" is meant a substantial retrogression of the roentgenographic shadows; by "marked improvement" is meant a retrogression of exudative processes and shrinking of cavities.] The chronic phase of the disease was present in 9 patients. Vionactan therapy resulted in slight improvement in 2 patients; there was no change in 2 other patients, and the condition of 2 became worse.

A combination of Vionactan and other antibiotics was given to 35 patients. Twenty patients (including 8 patients of the first group) received orally the combination of Vionactan and isonazid. Slight improvement resulted in 5 patients, marked improvement in 9, and radical improvement in 3; there was no change in 3 patients. The combination of Vionactan and aminosalicylic acid was administered by intravenous infusion to 13 patients. It brought about slight improvement in 2 patients, marked improvement in 5, and radical improvement in 2; there was no change in 4 patients. The combination of Vionactan and streptomycin was given to 2 patients. It resulted in slight improvement in one patient and no change in one. The patients tolerated Vionactan very well. A slight degree of albuminuria developed in all the patients, being the only observed sign of renal reaction to the drug. Headache and vertiginous disorders attributed to the 8th cerebral nerve were noted in 2 patients. Vionactan combined with either isoniazid or aminosalicylic acid gave excellent results in patients in the early phase of pulmonary tuberculosis, who had not previously received or had received only a small amount of other antibiotics. This combination gave good results in patients with chronic disease who had not previously received any chemotherapy, and it gave fair results in those chronically ill patients who had previously received other antibiotics. The authors suggest that Vionactan combined with either isoniazid or aminosalicylic acid can be usefully employed for the treatment of the early phase of pulmonary tuberculosis, or the chronic phase without previous chemotherapeutic treatment, whereas the combination with streptomycin and other antibiotics can be left for succeeding therapeutic management requiring a prolonged maintenance therapy.

Clinical Experiences with the New Broad-Spectrum Antibiotic Reverin Injected by Intravenous Route. K.-F. Albrecht. *Chirurg 29:445-448 (Oct.) 1958* (In German) [Berlin].

Reverin is the trade name given to a German preparation, pyrrolidinomethyltetracycline, which was developed by partial synthesis from pure tetracycline. This new tetracycline derivative shows in physiological pH areas a definitely improved solubility as compared with other tetracycline derivatives. The strength of its action and the broadness of spectrum are exactly equivalent to those of tetracycline hydrochloride. At the surgical clinic of the University in Marburg on the Lahn (Germany) this new broad-spectrum antibiotic was given by intravenous route to 174 either hospitalized or ambulatory patients. Some of these patients had inflammatory conditions, such as furunculosis, suppurative bursitis, empyema of joint cavities, osteomyelitis, diabetic gangrene, peritonitis after perforating appendicitis, perforation of stomach, ileus, acute pancreatitis, and pneumonia, or urologic infections (to the exclusion of those caused by Proteus organisms and Pseudomonas aeruginosa). Other patients with paraurethral abscesses, surgically removable sequestrums, phlegmons of the palm, and paronychia received Reverin as an adjuvant to surgical therapy. The drug was also administered in intracranial operations, surgical intervention on pharyngoesophageal diverticula, gastrointestinal resections, cholecystectomy, prostatectomy, mastectomy, recurrent hernia operations, ureteral bougienage, removal of renal and ureteral calculi, cystectomy, and urologic plastic operations, as well as in fractures of the base of the skull, for prophylaxis of infections.

In most of these patients one intravenous injection of 275 mg. of Reverin daily for 4 to 7 days was sufficient for therapeutic and prophylactic purposes. Patients with severe infections or with those caused by pathogenic agents with reduced sensitivity to tetracycline were given 2 daily injections, and occasionally 4 or 5 daily injections were given. One intravenous injection of 5 to 25 mg. per kilogram of body weight proved to be sufficient in children. The satisfactory local tolerance of the drug made it possible to perform the intravenous injection within one minute. The resulting high initial concentration in the serum of the patient is apparently of essential clinical significance. Signs of irritation were not observed in the veins even with repeated injections made into the same blood vessel. No undesirable side-effects were observed except for insignificant sensations of bitter taste on the tongue which occurred in 70% of the patients.

PATHOLOGY

Copper Metabolism in Normal Adults and in Clinically Normal Relatives of Patients with Wilson's Disease. F. C. Neale and M. Fischer-Williams. J. Clin. Path. 11:441-447 (Sept.) 1958 [London].

Increased copper content of the liver, brain, and other tissues, increased urinary excretion of copper, a decreased level of copper in the serum, and an associated decreased level of the copper-containing plasma protein coeruloplasmin are some of the biochemical abnormalities that are found in hepatolenticular degeneration (Wilson's disease). Aminoaciduria, not necessarily accompanied by an abnormal blood level of amino acids, is also found in hepatolenticular degeneration. This familial disease is inherited in a recessive, autosomal way. Biochemical abnormalities have occasionally been reported in clinically normal relatives of patients with hepatolenticular degeneration, namely, an excess aminoaciduria and a low coeruloplasmin level. The authors investigated the serum level and the urinary excretion of copper in 48 clinically unaffected relatives of patients with hepatolenticular degeneration.

The copper values obtained in serum and urine in these 48 persons are reported together with a control study of 106 normal adults. The urinary copper excretion was normal in all the relatives. The mean value for serum copper was found to be 100 mcg. per 100 ml. in normal males and 108 mcg. per 100 ml. in normal females, and this sex difference is statistically significant. Interpreted in the light of these control values, 35 of the 48 relatives had normal serum copper levels. Two child-bearing relatives showed high values. The parents of patients with hepatolenticular degeneration may be biochemically normal or abnormal. Eleven asymptomatic relatives showed low serum copper levels, and 5 of these were undoubtedly abnormal (47 to 70 mcg. per 100 ml.). Since half of these relatives were beyond the age at which hepatolenticular degeneration manifests itself, it may be concluded that some of the unaffected relatives have abnormally low serum copper levels.

Cutaneous Petechiae in Fatal Coronary Artery Disease. L. M. Gerlis. J. Clin. Path. 11:391-395 (Sept.) 1958 [London].

In the clinical recognition of myocardial ischemia, the nature and distribution of the referred pain which frequently accompanies it are of considerable diagnostic importance. Unfortunately in cases of sudden death there may be no such history, and not always is an unequivocal fatal cardiac lesion found, such as a recent or ruptured infarct or an acute occluding lesion of a coronary artery. In some there is little to indicate why or how the patient actually died, as the only cardiac lesions found are of long standing. In 7 autopsies in cases of acute coronary death, cutaneous petechiae were observed at sites commonly associated with referred pain of cardiac origin. No such lesions were observed in any deaths not of coronary origin. These petechiae were all outside the area of cutaneous postmortem hypostasis, and in no case was there any evidence of generalized hemorrhagic disease. It is suggested that this sign may be of diagnostic significance in the postmortem diagnosis of coronary insufficiency.

In the first patient presented, a 72-year-old woman, who died in a collapsed state with dyspnea and pain in the left shoulder 3 weeks after she had experienced an attack of gripping pain in the retrosternal region, autopsy revealed fine recent petechiae over the deltoid region and in the submammary region on the left side. The heart showed extensive recent infarction. Autopsy on another patient revealed a localized area of fine recent petechiae on the right side of the chest extending as a horizontal band, 7.5 cm. long and 5 cm. wide, just below the right nipple and fading out over the right border of the sternum. In still another patient small recent petechiae were seen over both shoulders and between the shoulder blades.

Two of the 7 patients had been subjected to frequent clinical examinations before death, but in neither case had cutaneous petechiae been noticed, nor have similar lesions been recorded among the clinical manifestations of coronary disease. Although fatal coronary disease is common, these petechiae are rare. Five of the 7 cases were from a personally studied series of 360 deaths due to coronary insufficiency in which a search for petechiae was specifically made, giving an incidence of 1.7%. These cutaneous petechiae may be caused by intense efferent stimuli along a sympathetic nerve pathway similar to that involved in referred pain, possibly by agonal relaxation of blood vessels which had been damaged by prolonged spasm. It is suggested that the presence of such localized petechiae is supporting evidence of acute coronary insufficiency, particularly in those cases in which the coronary arteries themselves show no recent culpable organic lesion. In 4 of the cases hemorrhagic lesions were found in direct relationship to the coronary arteries.

Simplified Technique of Cytodiagnosis in Cancers of the Esophagus: The "Wick" Procedure. C. Debray, J.-P. Hardouin, A. Deporte and E. Martin. Presse méd. 66:1451-1452 (Sept. 24) 1958 (In French) [Paris].

The somber prognosis of esophageal cancer and the seriousness of the therapeutic measures it requires make it essential to establish the diagnosis by histological study. Esophageal biopsy and cytodiagnosis, the diagnostic methods now in use, have certain disadvantages. Thus, esophageal biopsy often produces negative results, because, for one reason or another, the specimen was not correctly obtained, while cytological diagnosis as usually practiced by lavage of the lesion uses large quantities of fluid requiring special centrifuges and necessitates the examination of a great number of slides. These disadvantages are overcome by a simplified method involving examination of cells deposited by contact on a rough fabric—that of a cotton wick.

The originality of the wick method lies in the manner in which the specimens are obtained. An ordinary oil-lamp wick with a diameter just large enough to fit over a Camus sound is sterilized and fastened in place over the sound, close to the knob, with a few twists of linen thread. The patient, who must be fasting, is given a preliminary injection of promethazine, and the prepared sound is introduced gently, and usually without difficulty, into the esophagus until it reaches the stenosis. The whole procedure is managed under radioscopic control. The sound is then advanced through the stenosed segment with special care to avoid false routes or perforations. Sometimes the passage can be accomplished easily; sometimes the patient must help to carry it out by expedients such as turning or swallowing a little water, or an injection of atropine may be given; sometimes, again, the attempt must be abandoned, because in no case should force be used. When the stenotic area has been cleared, the patient lies down for an hour during which the sound, with its wick, remains in contact with the lesion. It is then withdrawn; the wick is slit lengthwise and laid out flat; and specimens of the adherent film of mucus are removed for study. The material is usually abundant and can easily be analyzed after Papanicolau staining. Several specimens must be taken, however, because the cells found, even in one lesion, will vary according to the area from which they were obtained. Thus, red blood cells will appear predominantly in one slide, inflammatory elements in another, and, finally, cancer cells in a third.

Utilization of this technique produced positive results in 12 of 18 patients with cancer and negative results in 6 with non-neoplastic lesions. The 6 failures were due in 3 cases to failure of the sound to clear the stenotic area—in one, to a technical error by which the cells failed to adhere to the slide; in one, to the fact that the cells were necrotic and could not be analyzed; and, finally, in one, to the fact that the cancer was submucosal and there was no change in the mucosa. The wick procedure was, therefore, successful in 86% of the cases in which the stenotic area was satisfactorily cleared, excluding the one last mentioned in which there were no mucosal changes.

Myocarditis with Endocardial Elastomyofibrosis (EEMF). E. R. Fisher and E. R. Davis. Am. Heart J. 56:537-552 (Oct.) 1958 [St. Louis].

The authors report on a 23-year-old Korean war veteran with myocarditis associated with severe endocardial elastomyofibrosis who died of cardiac failure about one year after the onset of the heart disease. Laboratory studies revealed a leukocytosis of 20,000 leukocytes per cubic millimeter, with 60% eosinophils, an elevated erythrocyte sedimentation rate, and hypochromic anemia. Ancylostoma and Ascaris ova were identified by stool examination, and a Trichinella skin test was positive on one occasion. There was a slight elevation of temperature to 100 F (37.8 C). In the earlier part of the patient's

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CAUSE OF PEPTIC ULCER

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Patients with duodenal ulcer are regularly found to have from 3 to 20 times the normal amount of hydrochloric acid in the fasting stomach at night. Such hypersecretion, when induced in dogs, regularly causes duodenal ulcers to form. Cutting the vagal nerve supply to the stomach reduces the fasting nocturnal secretion below the normal level. When the operation of vagotomy is combined with gastroenterostomy done in such a way as to prevent stasis of food in the pyloric antrum, the duodenal ulcers heal and remain healed. This has been demonstrated in 500 patients with duodenal ulcer. Gastric ulcer, however, most commonly arises in patients whose stomachs are atonic and display a fasting secretion less than normal. Stasis of food in the stomach causes excessive gastric secretion of humoral origin and consequent ulcer formation, while gastroenterostomy, which relieves the stasis, exerts a healing effect on gastric ulcers. Measurement of the nocturnal fasting acid secretion is therefore of great value in deciding whether the surgeon should perform vagotomy combined with antrum resection or gastric resection alone for gastric ulcers.

THE BELIEF that gastric and duodenal ulcers are caused by the digestant action of the gastric juice developed from the realization that these lesions occur only in those regions of the gastrointestinal tract that come in contact with the gastric secretion. It was supported by the discovery that medical measures which neutralize or dilute the hydrochloric acid of the gastric secretion exert a healing effect and that surgical procedures, such as gastric resection, which reduce the quantity of gastric secretion are also beneficial. Recent work in the laboratory and clinic has supported this view and has led to the widespread adoption of the term "peptic ulcer" for these lesions.

The older workers realized that, under normal conditions, the mucosa is not digested away, and so it seemed necessary to postulate that in patients with ulcers a local decrease in the resistance of an area of the mucosa must precede the digestion of the tissue. In the intervening years, it has been suggested that this decrease in resistance is brought about by thrombosis or embolism in the terminal branches of the gastric or duodenal arteries, by local vascular spasm, by local allergy, by decrease in the antienzyme content of the cells, by deficiency of protective mucus, or by general debility of the mucosa cells as a result of anemia, malnutrition, or specific vitamin deficiency.

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When resection of portions of the stomach for the treatment of peptic ulcer became popular, Konjetzny,[1] in Germany, examined the gastric and duodenal blood vessels in a large number of resected specimens but failed to find evidence of local arteriosclerosis, thrombosis, or embolism. In the experimental laboratory it was found that even extensive ligation of the gastric blood vessels did not produce lesions in the mucosa because of the abundant collateral circulation. When the critical point was exceeded, portions of the stomach became gangrenous but peptic ulcers were not produced. A similar result has been recorded in man when the blood supply to the stomach has been too greatly reduced in the effort to extend it high in the chest after resections of the upper part of the esophagus for carcinoma. Here again, when the critical point has been exceeded, necrosis of the stomach rather than peptic ulceration has resulted. In the surgical treatment of gastric and duodenal ulcers, local excision of the lesions was tried but found to be ineffective. New ulcers appeared in other areas. If the essential defect causing the ulcer was local thrombosis or embolism, excision of the involved area should have given a better result. Duodenal ulcer occurs predominantly in young and otherwise healthy adult males in whom evidence of arteriosclerosis, malnutrition, vitamin deficiency, or other systemic disease is not conspicuous. For these reasons it is exceedingly doubtful that a local decrease in resistance of the mucosa can account for any large number of the peptic ulcers seen in man.

The destructive effect of the gastric content is due to the concentration of hydrochloric acid and pepsin provided by the gastric juice. The other materials present, namely, swallowed food, saliva, mucus from the pyloric antrum, and regurgitated duodenal secretions, all exert a protective effect by buffering and diluting the gastric secretion. The key to the ulcer problem was provided by the discovery that pure gastric juice as it is secreted by the fundic glands has the capacity to digest and destroy all living tissue, including the mucous membrane of the jejunum, the duodenum, and the stomach itself. This central fact was made evident by the finding that the legs of living frogs are digested away if immersed in pure gastric juice obtained from accessory stomach pouches in dogs, that the drainage of pure gastric juice from such accessory stomach pouches into the empty small intestine regularly produces typical peptic ulcers, and that the totally isolated stomach with intact vagus innervation with abundant secretion regularly develops progressive peptic ulcers.[2]

While there can be no doubt that mucus and the anatomic folds of the gastric mucosa help to protect it from peptic digestion, these factors are less important than dilution and neutralization of the gastric juice secreted by the fundus. Several years ago, I[2] found that organs such as the spleen and kidney are not digested away if implanted into defects made in the gastric wall of dogs and subjected to the digestive action of the usual gastric content. If, however, these organs were transplanted into defects made in isolated stomach pouches where they were exposed to the digestant action of the pure fundic secretion, they were promptly digested away. One must conclude that, under normal conditions, the mucosa is not digested away because it is not exposed to pure gastric juice or to a content that resembles pure gastric juice in acid and pepsin concentration for any prolonged period of time.

In the intervals between meals, a continuous secretion of gastric juice in the empty stomach is regularly found in normal persons. This secretion is chiefly of nervous origin, and, in a 12-hour period at night, an average of 560 cc. of secretion with a free acidity of 30 clinical units may be aspirated from the stomach. The output of free hydrochloric acid varies between 15 and 20 mEq. With the ingestion of food, a profound augmentation in this secretion occurs, first, due to secretory impulses in the vagus nerves, aroused reflexly by the sight, odor, and taste of the food and, subsequently, due to the stimulating effect of the gastric secretory hormone gastrin, liberated from the antrum of the stomach as a result of gastric peristalsis and the contact between substances in the food and the antrum mucosa. If neutral or partially acidified food escapes through the pylorus into the duodenum, hormones are released from the duodenal musoca which also stimulate gastric secretion. This is the so-called intestinal phase of gastric secretion. When the pH of the gastric content reaches approximately 2.5 to 3, further secretion of gastric juice is inhibited. While the cause of this inhibition of gastric secretion is not finally settled, it appears to be due to the fact that acid of adequate concentration in contact with the antrum mucosa prevents the release of gastrin and that acid of adequate concentration in the duodenum releases from the duodenal mucosa a hormone which inhibits the secretion of gastric juice. It is interesting in this connection that fairly pure preparations of pancreatic secretin produced, when injected intravenously, a profuse secretion of pancreatic juice and a simultaneous inhibition of gastric secretion.[3]

If an excessive secretion of gastric juice occurs, it is readily apparent that the neutralizing and diluting effect of swallowed food, saliva, gastric mucus, and regurgitated duodenal secretions could eventually be overcome and there accumulate in the stomach a gastric content resembling pure gastric juice in pepsin and acid concentration. This should more readily be achieved if the secretion occurred in the empty stomach in the absence of the stimulating and also neutralizing effect of foodtaking. Several years ago, I proposed the concept that peptic ulcers are due to a hypersecretion of gastric juice rather than to a local decrease in the resistance of the mucosa. It was further suggested that the hypersecretion of gastric juice in patients with duodenal ulcer is usually of nervous origin, whereas the hypersecretion of gastric juice in those with gastric ulcer is usually of hormonal or humoral origin.[4]

Duodenal Ulcer

The evidence that duodenal ulcers are usually due to a hypersecretion of gastric juice of nervous origin may be summarized as follows: First, if adequate collection methods are employed, it has been found that patients with duodenal ulcer put out from 3 to 20 times as much hydrochloric acid in the fasting empty stomach at night as do normal persons. Measurement of the fasting night secretion in these patients has been a routine procedure at this clinic for the past 16 years. During this time, data have been secured on approximately 1,300 patients with various types of peptic ulcer. Most patients with duodenal ulcer put out between 60 and 70 mEq. of free hydrochloric acid during a 12-hour period at night, as compared with 10 to 20 mEq. by normal persons. Many patients with duodenal ulcer put out over 100 mEq., and two have been encountered who put out the remarkable total of 352 and 358 mEq. respectively. This hypersecretion is a good criterion of the severity of the ulcer problem and can be used as a guide for appropriate therapy. If the acid output is 50 mEq. or greater, the likelihood of medical management proving permanently successful is remote and surgical intervention is definitely indicated. On the other hand, if the acid output varies between 20 and 30 mEq., further trials with medical management should be undertaken.

Second, if a hypersecretion of gastric juice of the extent found in patients with duodenal ulcer is reproduced in dogs, ulcers of the duodenum regularly form. We are indebted to Hay and co-workers [5] for this highly significant experiment. A continuous hypersecretion of gastric juice was induced in dogs and other animals by implanting pellets of histamine in beeswax into the subcutaneous tissues. When the output of acid roughly approximated that found in patients with ulcer, typical progressive ulcers in the duodenum were produced. These observations have been repeatedly confirmed in the laboratory of the department of surgery at the University of Chicago as well as elsewhere.

Third, when the vagus nerves of the stomach are completely divided in patients with duodenal ulcer, the output of acid in the fasting nocturnal gastric secretion falls below the level found in normal people.[6] This fact, established in over 1,200 patients subjected to vagotomy for duodenal ulcer in the University of Chicago surgery clinic, together with a great many elsewhere, constitutes strong evidence that the fasting hypersecretion of gastric juice in patients with duodenal ulcer is of nervous origin. It is attractive to speculate that in some way the stresses and strains of modern life produce a secretory hypertonus in the vagus nerves and, thus, that the central nervous system plays an important role in the disease. For a long time, physicians have called attention to the high incidence of duodenal ulcer in persons whose occupations subject them to long continued anxiety, competitive effort, and mental strain. The lesion has been referred to as a wound stripe of civilization and as a psychosomatic disease.

The postulate that the hypersecretion of gastric juice in patients with duodenal ulcer may be in part due to the hypothalamus-anterior pituitary-adrenal stress mechanism has not been supported by work in this laboratory.[7] While it may be conceded that physical stress, and possibly also mental stress, is accompanied by the increased elaboration of ACTH and cortisone into the blood stream, these substances do not stimulate gastric secretion sufficiently to be effective in the production of peptic ulcers. In a series of patients with duodenal ulcer in whom the fasting night secretion was determined for several days before operation and also for the first five or six days of the postoperative period, interesting results bearing on this question were obtained. Almost uniformly, the fasting secretion of the patient with duodenal ulcer was markedly increased on the night before the operation. This could probably be due to the anxiety experienced by most patients concerning the coming surgical ordeal. During the first five days after the operation, the output of hydrochloric acid in the fasting 12-hour night secretion remained below 10 mEq. This indicates that hypersecretion characteristic of duodenal ulcer is abolished by vagotomy and, further, that the trauma of operation does not stimulate the secretion of gastric juice in the vagotomized stomach.

Fourth, when the vagus nerves to the stomach in patients with duodenal ulcer are completely divided and when this operation is combined with an effective drainage procedure so that stasis of food in the antrum of the stomach is prevented, the duodenal ulcers heal and remain healed. A good deal of controversy about this operation has developed both in the United States and abroad. This controversy has almost always revolved about a comparison of the relative efficiency of vagotomy and gastroenterostomy as compared with subtotal gastric resection as a method of treatment. No one seems to have questioned the observation that division of the vagus nerves exerts a markedly beneficial effect on the healing of duodenal ulcers. In my experience, this has been directly parallel to the reduction in the fasting secretion of gastric juice produced by the operation.

Operation for Duodenal Ulcer

A few words concerning the conduct of the operation itself and the aftercare of patients treated in this way may prove useful. In the selection of patients, those with objective evidence of crater or duodenal deformity sufficient to account for subjective symptoms are apt to give the best results. This is particularly true if the fasting night secretion of free hydrochloric acid exceeds 50 mEq. Vagotomy combined with a drainage procedure should not be done in women unless there is fluoroscopic evidence of a crater as well. It is a misconception to regard vagotomy as an operation for nervous patients. Vagotomy is no more effective in the treatment of psychoneurosis than is gastric resection.

On the night before the operation, a small rubber tube is introduced through the nose into the stomach and the gastric content recovered by aspiration for a 12-hour period. When compared with previous estimates, it will usually be found that on the night before the operation the patient secretes 50% more hydrochloric acid than at other times.

General anesthesia with good relaxation is necessary. The abdomen is opened by a high midline or left paramedian incision. The abdominal organs are explored, and if a duodenal ulcer is found the operation is continued. The omentum is packed to one side by a laparotomy pad placed below the spleen. While the surgeon pulls down on the left lobe of the liver, his assistant divides the suspensory ligament. The left lobe of the liver is then retracted at the right and the upper part of the stomach exposed. The center of the esophagus is identified by palpating the rubber tube, and a short incision is made through the diaphragm about 1 cm. above the hiatus or midway between the esophageal hiatus and the transverse diaphragmatic vein.

It is my practice to make a small opening in the diaphragm with scissors and to enlarge this opening by blunt dissection in an attempt to avoid troublesome bleeding. If the opening is made immediately over the esophagus, there is little danger of opening the pleura. The fingers are then introduced into the mediastinum, gently separating the esophagus from the surrounding tissue. The fingers are then swept around the esophagus, picking up all of the vagus fibers and pulling these together with the lower part of the esophagus through the opening into the abdomen. Great care must be observed not to insinuate the fingers between the right vagus trunk and the esophagus or the trunk will be pushed aside and missed. The main trunks are easily separated from the esophagus by finger dissection, and a segment 2 to 3 cm. in length is excised between ligatures of silk or linen. After the main trunks have been divided, a forceps is used to pick off all strands of fascia, small blood vessels, or nonyielding strands which may represent nerve fibers. When this is completed, the lower 2 in. of the esophagus is denuded of all tissue, exposing the bare longitudinal esophageal musculature. Occasionally, a nerve fiber must be pried out of the esophageal muscular wall. With the fingers of the right hand in the mediastinum, it is possible by downward traction on the stomach to make sure that no fibers passing to the lesser curvature are overlooked.

The esophagus is then permitted to fall back into the mediastinum, and the opening in the diaphragm is closed with two interrupted catgut sutures. The left lobe of the liver is permitted to fall back in place, but the ligament is not restored. If the pylorus is not too greatly deformed by scar tissue or distorted by the hyperemia and edema of a large penetrating ulcer, a pyloroplasty of the type described by Weinberg is then carried out. A short longitudinal incision is made in the stomach midway between the greater and lesser curvatures and extending to the pylorus. If the finger is then introduced through the pylorus into the duodenum, the presence of obstruction can be determined and the incision extended into the duodenum past the involved area. A corresponding length of incision is then made in the stomach and the opening closed transversely with a single layer of interrupted silk sutures placed approximately 3 mm. apart. Infolding of the suture line should not be done, but omentum may be placed over the incision if desired. A stab wound is then made in the body of the stomach near the greater curvature, a Foley catheter inserted, and the bag filled with 15 cc. of water. The stomach is infolded about the catheter with two pursestring catgut sutures. Omentum is then wrapped around the catheter, and it is brought out to the left of the incision just below the costal margin. The catheter is then pulled upward to bring the stomach and omentum snugly against the abdominal wall. Gauze tied about the catheter holds it in place for 24 to 48 hours or until adhesions have formed.

The stomach is decompressed by means of this Foley catheter gastrostomy for five days. During this time, it is wise to collect a 12-hour night secretion and determine the output of free hydrochloric acid as was done before the operation. If the vagus nerves have been successfully divided, the output of acid is usually less than 10 mEq. Gastrostomy decompression of the stomach is much more acceptable to the patient than is decompression by an esophageal tube. There is also a decreased incidence of pulmonary complications.

It is my practice to leave the Foley catheter in place until the patient leaves the hospital. On the sixth day, gradual feeding with liquids followed by semisolid foods begins and increments are made in the diet, guided by satisfactory emptying as evidenced by aspiration on the catheter in the evening. When the catheter is pulled out on the 10th or 11th day, the stab wound heals promptly without leakage of gastric content. The patient is then instructed to eat small meals for the first three or four weeks and to stop eating if sensations of distention appear. With this prolonged period of decompression and gradual resumption of food-taking, almost all patients remain comfortable and the formerly noted complications of belching, sensations of distention, and diarrhea have not occurred. These are apparently due to stagnation of food in a relatively anacid stomach which permits bacterial fermentation. As the acid production by the stomach is markedly reduced, bacteria normally found in the colon and lower ileum migrate higher in the gastrointestinal tract and may even become established in the stomach. If decompression has been inadequate to permit resumption of normal gastric motility, antibiotics such as succinylsulfathiazole (Sulfasuxidine) or oxytetracycline (Terramycin) may be used to restrict bacterial growth. The oral administration of dilute hydrochloric acid before and after meals is also helpful in these patients.

A careful follow-up study is advisable, and all patients should return to the hospital after six months for a measurement of the fasting night secretion and an x-ray examination of the stomach to determine the degree of healing and whether stasis of food in the antrum exists. In this connection it is wise to take x-ray pictures at intervals of six and eight hours after the administration of the barium meal. Simple demonstration that barium leaves the stomach by way of the new opening is not sufficient. If the fasting night secretion has been reduced below the level found in normal persons and if stasis of food in the stomach is not present the probabilities are great that the patient will remain free of his disease.

In the first 500 patients with duodenal ulcer treated by vagotomy and gastroenterostomy in this clinic in whom the follow-up period has been five years or more, 90% received a good to excellent result. They were relieved of ulcer symptoms and objective evidence of ulcer and were able to eat a normal diet without medication. Only 0.4% died from the operation, and failure to secure a good clinical result was usually due to incomplete vagotomy, an inadequate drainage procedure, or both. In this connection it was found that a gastroenterostomy with the stoma located in the body or fundus of the stomach often did not prevent stasis of food in the antrum of the stomach. This was particularly evident in patients with high-grade pyloric stenosis in whom x-ray examination might reveal barium in the antrum distal to the gastroenterostomy stoma from 9 to 12 hours after ingestion of the meal. Careful appraisal of results after these factors have been recognized will probably reveal fewer failures.

Gastric Ulcer

The evidence that gastric ulcers are usually due to a hypersecretion of gastric juice of humoral or hormonal origin derives in part from experimental studies on the mechanism of gastric secretion and in part from reflections on the results of surgical treatment of peptic ulcer. Laboratory studies have established the validity of Edkins' theory, which holds that food in the stomach stimulates gastric secretion by causing the manufacture and release of a hormone, gastrin, from the antrum of the stomach which passes into the circulation and stimulates the secretory activity of parietal cells in the corpus and fundus of the stomach.

It has been further demonstrated that not only contact of the antrum mucosa with food but also intragastric tension, such as that provoked by antrum peristalsis or contraction, is also a potent stimulus for the release of gastrin. Indeed, contact of the antrum mucosa with food plus the stimulating effect of antrum contractions is a more effective stimulus than either factor alone. Both become ineffective when the gastric content becomes acid in reaction.

There is some disagreement concerning the mechanism by means of which the increasing acidity of the gastric content inhibits further gastric secretion. Some hold to the view that under these conditions an inhibitory hormone is released from the antrum mucosa.[8] Experiments in this laboratory support the view that acid in contact with the antrum mucosa prevents the release of gastrin, possibly in a manner similar to that produced by cocainization of the mucosa.[9] When neutral or faintly alkaline food enters the duodenum, stimulation of gastric secretion results, mediated by the release of a gastrin-like hormone from the duodenal mucosa. This is the so-called intestinal phase of gastric secretion. When, however, the material leaving the stomach is definitely acid in reaction, the contact of this acid food with the duodenal mucosa brings about an inhibition of gastric secretion through the liberation of an inhibitory agent from the duodenal mucosa. In this connection, it is interesting that preparations of pancreatic secretin suitable for intravenous use in man, when given to animals, produce a vigorous secretion of pancreatic juice and a simultaneous inhibition of gastric secretion. This preparation of pancreatic secretin is not a pure substance, so the possibility remains that a second chemical fraction is present which specifically inhibits the release of gastrin from the antrum.

Comment

These data permit the following summary. Under normal conditions a constant or continuous secretion of gastric juice occurs in the empty human stomach even though the patient is shielded from the sight, odor, or taste of food. The amount of acid in this secretion varies between 10 and 20 mEq. in a 12-hour period at night and is largely nervous in origin, as indicated by the fact that it is almost completely abolished by division of the vagus nerves to the stomach. A marked augmentation in gastric secretion occurs with the ingestion of food, brought on in part by secretory impulses in the vagus nerves aroused reflexly by the sight, odor, and taste of food. The entrance of food into the stomach initiates gastric peristalsis, which brings food in contact with the antrum mucosa. Gastric secretion initiated by vagus impulses is continued by the stimulating effect of gastrin. It is likely that in many patients at the beginning of the meal some neutral or faintly acid food escapes through the pylorus. This would cause the liberation of a gastrin-like hormone from the duodenal mucosa, and for a short time this intestinal phase of secretion is operative. However, when the acidity of the gastric content becomes optimal for peptic digestion, further release of gastrin from the antrum ceases and the acid chyme entering the duodenum provokes the liberation of pancreatic secretin, which stimulates pancreatic secretion and also inhibits further secretion of gastric juice. It seems clear that, in this mechanism, stimulation of gastric secretion adequate for gastric digestion is provided, and there are also factors which limit secretion and protect the mucosa against its corrosive action.

In experimental animals, a hypersecretion of gastric juice of hormonal origin sufficient in extent to produce typical, progressive ulcers in the stomach, duodenum, or jejunum can be induced by transplanting the antrum into the colon as a diverticulum.[10] The cause of this hypersecretion appears to be the liberation of gastrin from the transplanted antrum provoked by the peristaltic activity of the colon and continuing because the colon content does not become acid in reaction. In this new situation, the acid cut-off mechanism which operates when the antrum is in its normal location is absent. It may well be that the potent ulcerogenic action of the excluded antrum after the Finsterer-Devine operation is due to a similar cause. Food regurgitating through the duodenum and into the excluded antrum is apt to be neutralized by duodenal secretions and so provide a continuing stimulation for gastrin release. Stasis of food in the stomach appears to be the event in human pathology most likely to cause a prolonged or excessive secretion of gastric juice of humoral origin. Stasis of food plus hypermotility of the stomach probably occur in most patients with duodenal ulcers which produce pyloric stenosis. The secondary development of gastric ulcers in such patients has long been known [11] and can be attributed to an excessive secretion of gastric juice caused by prolonged liberation of gastrin from the antrum as a result of both contact with food and antrum hypermotility.

Experimental evidence indicates that pyloric stenosis in dogs will produce a hypersecretion of gastric juice of humoral origin sufficient in degree to be ulcerogenic.[12] It is quite likely that this factor of pyloric stenosis brought about by organic changes or by spasm may be an additional factor in many patients with ulcer. The initial hypersecretion is of nervous origin, the lesion is produced, pyloric stenosis then develops, and, as a result of this, there is a further stimulation of gastric secretion of humoral origin. It seems likely that only about 20% of gastric ulcers occur in patients with previous duodenal ulcers producing stenosis at the pylorus. In the remainder, stasis occurs as a result of gastric atony. These patients display a fasting gastric secretion of less amount than in normal people, and this may indicate a decreased tonus of the motor and secretory fibers in the gastric vagi.

Experience from the clinic supports these concepts. Gastroenterostomy, which relieves gastric stasis, exerts a healing effect on gastric ulcers, and resection of the antrum, as in the Kelling-Madlener operation, will usually bring about healing of a benign gastric ulcer in the region of the esophagus which has been left in situ. When gastroenterostomy or low gastric resection were employed in the treatment of duodenal ulcer, a relatively large number of these patients developed secondary gastrojejuna ulcers. As a result of this experience, resection o from two-thirds to three-fourths of the stomach ha become the more common procedure. When, however, gastroenterostomy or low gastric resection was employed in the treatment of gastric ulcer very few secondary gastrojejunal ulcers formed.

A rational explanation for these phenomen would seem to be that in patients with duodena ulcer the cause of the hypersecretion of gastri juice is of vagus or neural origin and is not corrected by gastroenterostomy or excision of th antrum, and, as a consequence, new ulcers form in the exposed gastrojejunal mucosa because of contact with the excessively acid gastric content. On th other hand, when the antrum is resected in patient with gastric ulcer, the cause of the hypersecretion of gastric juice is removed and for this reason secondary gastrojejunal ulcers do not form. The beneficial effect of gastroenterostomy in the latter may be attributed to the relief of stasis which prevent the abnormal or continued liberation of gastrin previously caused by prolonged contact of food with the antrum mucosa.

It is quite possible that the few gastrojejuna ulcers that have been encountered after gastroenterostomy or gastric resection for gastric ulcer have actually occurred in patients who have had both a gastric ulcer and a preexisting duodenal ulcer. In these patients it seems likely that the duodenal ulcer developed first as a result of a hypersecretion of gastric juice of nervous origin, and, subsequently, because of pyloric stenosis and retention of food in the stomach a hypersecretion of gastric juice of humoral origin was superimposed. In such a patient, resection of the antrum or, indeed, a gastroenterostomy might relieve the hypersecretion of gastric juice of humoral origin, but the hypersecretion of nervous origin would persist and so the patient would be liable to the development of a stoma ulcer. It is in a situation such as this where measurement of the fasting night secretion is of great value. The night secretion seems to be almost entirely of nervous origin, and, *if it exceeds 20 mEq. of hydrochloric acid in a* 12-hour period, vagotomy combined with antrum resection should be performed rather than gastrectomy alone.

Summary

The idea that peptic ulcers are due to a local decrease in the resistance of the mucosa to the digestant action of the gastric content has failed to receive either clinical or experimental support. On the other hand, it has been demonstrated that pure gastric juice, as it is secreted by the fundus of the stomach, has the capacity to digest all living tissue, including the muscosa of the stomach and duodenum, and to produce a defect which closely resembles progressive peptic ulcer as encountered in clinical practice. A gastric content resembling pure gastric juice is present in patients who secrete such large volumes of gastric juice that the neutralizing effect of food and alkaline secretions is overcome.

Peptic ulcers are usually caused by a hypersecretion of gastric juice rather than a local decrease in the resistance of the mucosa. The hypersecretion of gastric juice in patients with duodenal ulcer is of nervous origin, whereas in those with gastric ulcer it is usually of humoral or hormonal origin. Evidence from both the laboratory and the clinic supports these concepts. Gastrojejunal ulcers develop after low gastric resection for duodenal ulcers because the cause of the hypersecretion is nervous and is not corrected by excision of the gastric antrum. The relative absence of gastrojejunal ulcers after low gastric resection for gastric ulcer is attributed to the fact that removal of the antrum abolishes the cause of the hypersecretion of gastric juice in these patients.

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TIC DOULOUREUX.—Neurosurgeons have been reluctant to inject alcohol into the gasserian ganglion or root, because of the risk to ophthalmic fibers and to other cranial nerves. However, in the hands of some experts the procedure seemed satisfactory. . . . Preliminary radiographic study determines the entry point of the needle and the exact position of the head required. Then the needle is inserted vertically downward. Further radiographic study indicates the precise relation of the needle to the base of the skull and permits accurate adjustment of its depth. Procaine (2 per cent, 0.03 cc.) is injected to determine the position of the needle within the posterior root (pars triangularis); the needle is further adjusted if necessary. The patient's neck is straightened so that he faces the ceiling squarely. Finally from one to six therapeutic injections of 0.05 cc. of absolute alcohol are made, guided by careful sensory and motor testing. The goal is to prevent further attacks of pain with the least sensory loss. This procedure requires patience, cooperation, and a precise knowledge of anatomy. Over a period of 36 months we have found it safe and effective in relieving tic douloureux *in 45 consecutive patients.*—Arthur Ecker, M. D., and Theodore Perl, M. D., Alcoholic Gasserian Injection For Relief of Tic Douloureux, *Neurology*, June, 1958.

ATRIAL SEPTAL DEFECT—RESULTS OF SURGICAL CORRECTION IN ONE HUNDRED PATIENTS

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One hundred consecutive patients, ranging in age from 10 months to 45 years, with a diagnosis of atrial septal defect secundum, were operated on. Of the 100 patients, 38 were asymptomatic, 29 mildly incapacitated, 23 moderately incapacitated, and 10 severely so. Only eight gave a history indicative of congestive cardiac failure. The most prominent complaints were shortness of breath, fatigue, and palpitations (pounding in the chest). Operation was performed under conditions of hypothermia and inflow-outflow occlusion. After the second year of life, the earlier the operation is performed the better. Surgery in a relatively asymptomatic child between the ages of 2 and 10 years carries a minimum of risk and in all probability will insure a normal cardiovascular system when maturity is reached. A high pulmonary vascular resistance increases the risk and decreases the gain that can be anticipated from operation.

The indications for operation in a given condition depend inevitably on the risk of the procedure as weighed against the potential gain from its success. When the procedure is known to be curative and the risk steadily diminishes as experience is gained, a point is eventually reached when the diagnosis of the lesion becomes a firm indication for its correction. That point was arrived at several years ago in the case of the atrial septal defect. We here report the results of operation, based on this precept, in 100 consecutive cases.

The patients ranged in age, at the time of surgery, from 10 months to 45 years. There were 68 females and 32 males in the series. Some were without symptoms, while others were severely disabled. Likewise, the physical and other findings varied from normal to gross derangement.

Preoperative Evaluation

The assessment of the patient's condition was based on history, physical examination, electrocardiography, fluoroscopy, and, in many cases, cardiac catheterization. It is believed that the diagnosis can be achieved accurately on clinical grounds in over 90% of patients in the age group covered by this report, except, of course, the recognition of anomalous pulmonary venous connections.

It is also considered that the common atrioventricular lesion can be distinguished clinically; none of the patients operated on with the diagnosis of atrial septal defect secundum was found to have the former lesion.[1]

History.—The variability of symptoms in atrial septal defect has been frequently emphasized. In this series, incapacity in some patients was severe and in others it was absent. Though there were obvious exceptions, by and large the symptoms appeared in the third decade. Before that they were either absent or slight in most instances. The most prominent complaints were shortness of breath, fatigue, and palpitations ("pounding in the chest"), though there were a number of other symptoms expressive of ill health in general rather than heart disease in particular. Of the 100 patients, 38 were asymptomatic, 29 mildly incapacitated, 23 moderately incapacitated, and 10 severely so. Only eight gave a history indicative of congestive cardiac failure. We did not find a marked increase in the incidence of respiratory infection in these patients, nor did we note a predilection for rheumatic fever.

Physical Signs.—The classic slight build (gracile habitus) was noted in most of the children in this series, and sometimes this was particularly marked. However, it was by no means an invariable finding; a few of the older patients were, in fact, stocky rather than slender.

The normal or small arterial pulse was in most cases in sharp contrast to the marked hyperactivity of the precordium. However, as with so many other findings, this activity tends to be much more pronounced and obvious in the young patient when the chest wall is very thin and less marked in the adult when it is thick. The venous pulse was not considered uniformly remarkable, though when tricuspid insufficiency was present the characteristic systolic wave was seen. A left precordial bulge was present in 40 patients. A systolic thrill was felt in seven, and in most patients the increased activity of the hyperdynamic right ventricle was detectable on palpation to the left of the sternum. Over the pul-

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monary area there was usually a systolic thrust, followed by a shock due to pulmonary valve closure —again, particularly in the younger patients.

A systolic murmur, most prominent in the second or third left intercostal space, was heard in every patient. It was rarely loud or harsh but was rather of the quality of the "flow-murmur." This murmur, resulting from functional stenosis of the pulmonary valve, was easily distinguished from the high-pitched, blowing, pan-systolic murmur of tricuspid insufficiency. The latter was heard in 10 patients, usually at the lower sternal edge. A short, early, low-pitched, diastolic murmur due to increased blood flow through the tricuspid valve was audible in 51 patients, and a high-pitched, blowing, diastolic murmur signifying pulmonary insufficiency was found in 5.

In no case was the diagnosis of Lutembacher's syndrome (atrial septal defect with mitral stenosis) seriously considered, nor was a true pulmonary stenosis suspected in any case.

The second sound was widely split and fixed with respect to the respiratory cycle in almost all patients who did not have a raised pulmonary vascular resistance. In the latter event it was louder and the split was narrower; at least this was the impression on auscultation.

Electrocardiogram.—The electrocardiogram showed all gradations from normal "crista supraventricularis pattern," through "right ventricular outflow tract hypertrophy," to undoubted "right ventricular hypertrophy."[2] We believe that the rSR′ complex so frequently found in patients with atrial septal defect secundum is a manifestation of right ventricular outflow tract hypertrophy or dilatation and that it is not due to a conduction defect. This subject will be dealt with in greater detail in another paper. In only one case was the electrocardiogram normal for age.

Fluoroscopy.—Fluoroscopy was, in this series, an indispensable part of the diagnostic study. Together with examination of the x-ray films, it provided valuable information. Several features were found to be particularly helpful. The vascular markings of the lung fields were accentuated and noted well out to the periphery. The heart was enlarged, as were the main, left, and right pulmonary arteries. The increased activity of these structures was also obvious, in contrast to the lack of prominence of the aorta, left atrium, and left ventricle. Taken together, these features make up a pattern which becomes quite characteristic of atrial septal defect; departure from it at once arouses suspicion of either an additional lesion or a different diagnosis.

In this series, the heart was enlarged in 95 cases, sometimes slightly and sometimes massively, though in most cases the enlargement was considerable. In all cases except one, the typical outline of the atrial septal defect was seen.

Cardiac Catheterization.—Early in the development of our understanding of the diagnostic pattern, cardiac catheterization was used as an aid to diagnosis and provided a wealth of data with which the postoperative findings could be compared. Ninety-three patients were studied in this fashion before operation, either at this center or at others prior to referral here. At the present time, catheterization is not performed unless there are specific features which require clarification.

Selection for Operation

On the basis of the considerations outlined briefly above, 100 patients were operated on, each with the diagnosis of atrial septal defect secundum. Two patients were given diagnoses preoperatively of patent ductus arteriosus in addition and eight of anomolous pulmonary venous connections. These lesions were found to be present in each case. Another seven patients were found at operation to have anomalous pulmonary venous connections previously undiagnosed. No cases of the Lutembacher syndrome or of pulmonic stenosis were found.

When the patient is between the ages of 2 and 45 years, the diagnosis of an uncomplicated atrial septal defect is a firm indication for operation. In older patients, other factors tend to weigh more heavily and must be carefully considered before operation is strongly advised. In the younger groups the problem of when not to advise operation is a more difficult one and is centered largely on the level of the pulmonary vascular resistance. The higher this is, and the lower the pulmonary blood flow, the higher is the risk of operation and the less the gain. We believe that the ideal time for operation is when the patient is between the ages of 2 and 10 years, the risk then being minimal and the gain from successful surgery the greatest. With the period of maximum growth still to come, obliteration of the defect gives such patients an excellent chance to have a completely normal circulatory system in adult life.

Operation was performed under conditions of hypothermia and inflow-outflow occlusion, according to techniques previously described.[3] No longer is there any doubt of the superiority of open-heart surgery in the handling of this lesion. It is essential that the exact relationships between the defect and the orifices of the various vessels entering the atriums should be accurately assessed visually. Since the success of the procedure depends on the reestablishment of a completely normal circulation, we are certain that direct vision is vital. Whether this is achieved by the use of hypothermia or the extracorporeal circulation is outside the scope of this article, and opinions will vary from center to center.

Results

Operative Mortality.—Seven patients died as a direct consequence of operation, all in the first 43 cases. There were no operative deaths in the succeeding 57 cases. Three patients died from postoperative thrombosis (one of pulmonary embolism, one of internal carotid artery thrombosis, and one of internal jugular vein thrombosis). One patient died as a result of postoperative bleeding; two patients with a high pulmonary vascular resistance died a few days after operation from congestive cardiac failure. In the remaining case, the cause of death was not clear. The changes in blood-clotting mechanisms during hypothermia and anesthesia are discussed by von Kaulla and Swan.[4] It is felt that cooling to below 30 C (86 F) greatly increases the liability to these complications and also that the early postoperative institution of anticoagulant therapy, as soon as sanguineous drainage from the chest tubes has ceased, minimizes the risk of thrombosis. Of the seven patients who died, four were "good risk" patients and three "poor risk," having a high pulmonary vascular resistance.

One other patient, aged 39, died at home eight weeks after operation. The cause of death is said to have been a cerebellar hemorrhage; she was receiving anticoagulant therapy at the time. Of the remaining 92 patients, we have recent information on 91.

Postoperative Assessment.—The success of operation is measured by the changes which occur after operation in symptoms, signs, electrocardiogram, radiologic findings, and, in 44 patients, postoperative catheterization. If the defect has been completely closed, the results of evaluation by all these methods show that there has been regression toward normal. If this regression does not occur within a few months, the question must at once be asked: "Why not?"

Eighty-one patients are considered cured by all methods of evaluation. Three others are clinically cured; normal regression of symptoms, signs, electrocardiographic findings, and heart size occurred after operation, but postoperative cardiac catheterization in these three still showed some left-to-right shunt at the atrial level. One of these patients was the last on whom interrupted sutures were used to close the atrial defect, and it is possible that some small gaps remain between sutures. One patient may still have a pulmonary vein draining into the right atrium. The third also had before operation anomalous pulmonary venous connections into the right atrium. In none of these three patients is the shunt of any apparent hemodynamic importance.

Two patients have left-to-right shunts at the atrial level which are of consequence. One is a 12-year-old boy; he was operated on in August, 1954. Postoperative catheterization showed complete obliteration of the shunt, and he has remained without significant symptoms. However, the electrocardiogram failed to reveal any regression toward normal and further catheterization recently has revealed that there is now a shunt. He was also a patient in one of the early cases, on whom interrupted sutures were used. The other patient is a 45-year-old woman with an extremely large heart and tricuspid insufficiency but a low pulmonary vascular resistance. Repeated catheterization seven months after operation showed persistence of the shunt at the atrial level, and she is unimproved.

One patient, now aged 18, did well in all respects for 18 months after operation but since then, over the succeeding two years, has become progressively more disabled by dyspnea and fatigue, accompanied by the development of central cyanosis and finger clubbing. The cause of this has recently been established to be the shunting of inferior vena caval blood directly into the left atrium.

Two patients have been troubled by postoperative arrhythmias. One of these, aged 37, has palpitations and some dyspnea on effort due to atrial flutter. The other, aged 31, had a grossly enlarged heart at operation and had been in cardiac failure. In her case, the arrhythmia has been inimical to her progress. Our latest report, six months after surgery, indicates that she is now improving.

One patient, aged 18, also had a large heart preoperatively and still has some breathlessness on effort one year after operation. However, he has shown improvement. Finally, a housewife 33 years of age, who had severe pulmonary vascular changes before operation, has shown no regression of her pulmonary hypertension in the nine months since operation, despite successful closure of her atrial septal defect. Though she says that she feels better, she is still mildly incapacitated and shows no objective evidence of improvement.

Thus, of the 91 patients of whom we have recent information, only 4 give grounds for serious concern, 2 due to the persistence of a significant left-to-right shunt, one due to the development of central cyanosis, and one due to the presence of apparently irreversible pulmonary vascular disease.

Summary

At the present time, 125 patients with an atrial septal defect of the secundum type have been operated on at this center under conditions of hypothermia, inflow-outflow occlusion, and direct-vision open-heart surgery. This report briefly analyzes the experience gained in the first 100 consecutive cases.

There were seven deaths due to surgery, all in the first 43 patients. In the last 82 patients there have been no deaths. The indication for operation,

in patients under 45 years of age, is the diagnosis of the uncomplicated anomaly. It is considered that, after the second year of life, the earlier the operation is performed the better. Surgery in a relatively asymptomatic child between the ages of 2 and 10 years carries a minimum of risk (less than 2%) and in all probability will ensure a normal cardiovascular system when maturity is reached.

With use of current methods, closure of the defect is almost assured. Only a small proportion of patients were not improved subjectively or objectively. A high pulmonary vascular resistance increases the risk and decreases the gain that can be anticipated from operation.

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PREGNANCY IN THE PATIENT WITH ILEOSTOMY AND COLECTOMY

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Surgeons have been reluctant to perform ileostomy for intractable ulcerative colitis in young women because the existence of the ileostomy was believed to militate against pregnancy and subsequent parturition. This belief is unsettled by a study of seven patients with ileostomy and colectomy. In all there were 13 subsequent pregnancies, of which 3 terminated in early spontaneous abortions while 10 went on to term and resulted in live births. In 9 of the 10 term pregnancies the patient was delivered per vaginam, and only one had to be delivered by cesarean section. There was no maternal mortality. In the past, unpredictable exacerbations of ulcerative colitis have been a serious danger in pregnancy. The experiences here recorded show that young women with otherwise intractable colitis can be treated by ileostomy and colectomy without fear of subsequent inability to bear children.

To deny a young woman the right to have a baby is a severe sentence to hand down. For the childless woman the effect of such a decision may be irreparable psychological trauma. The existence of an ileostomy per se does not warrant such a sentence. Our experience with the patient after ileostomy and colectomy leads us to the conclusion that she may undergo pregnancy and delivery without undue risk. The type of delivery is dictated not by the existing ileostomy, but by those factors which decide the type of delivery in any obstetric patient.

Although pregnancy complicated by idiopathic ulcerative colitis does not fall within the scope of this discussion, it seems pertinent to point out the following facts. Pregnancy brings about adverse and unpredictable effects in the majority of instances. These patients must be watched very carefully, and it may become necessary to interrupt the pregnancy in the interest of the life of the mother. There seems to be less chance of an exacerbation of the disease the longer it has been quiescent before the onset of pregnancy; however, the risk of a flare-up is always present. We feel that pregnancy should be discouraged in those women in whom the disease is moderately active. Abramson and co-workers[1] made similar observations and reported a fairly high mortality in the puerperal period. Bacon[2] in his recent and excellent treatise on ul-

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cerative colitis reviewed the literature thoroughly and concluded that, although the colitis may have little effect on the pregnancy itself, the pregnancy may cause severe and unpredictable effects on the colitis.

During the past 15 years ileostomy or ileostomy and colectomy have been done more and more frequently in uncontrolled cases of ulcerative colitis with its various complications. Quite obviously then, we shall encounter many young women who have had such surgery and who are desirous of having children. Our advice should mean much to them and particularly to the childless woman. Certainly, the presence of an ileostomy does not make it more difficult for her to become pregnant. In fact, the improvement in her general health after an ileostomy and colectomy may increase her chances of becoming pregnant.

The most likely questions from these women will be: 1. After this surgery can I, with a fair degree of safety, go through pregnancy? 2. What are the chances of difficulty with the ileostomy? 3. Do I need special care during the pregnancy? 4. What type of delivery may I anticipate? To answer these questions honestly and intelligently each of us needs to keep accurate records of such patients coming under our care and to report our results.

We have advised those young women who have ulcerative colitis and who are contemplating marriage that they can expect a normal rate of conception after excision of the colon and the rectum. Because of the possibility of the uterus becoming fixed in retroversion, one of us (R. K. G.) has made it a practice to fix the fundus with two mattress sutures of 00 absorbable chromic surgical suture (catgut) to the lower end of the incision in the anterior abdominal wall. Also, at the time of reconstruction of the pelvic peritoneal floor, we have made certain that both tubes and ovaries lie free within the abdominal cavity. Each of our young women so treated has become pregnant, and has been able to care for her children and household duties.

During the past seven years all of our operations have been ileostomy, total colectomy, and abdominoperineal resection of the rectum in one stage. The ileostomy has been constructed with a short rosebud with mucosa to skin sutures.

The rectovaginal fistulas so commonly seen in these patients before resection have healed and have given no trouble at the time of delivery. Partial intestinal obstruction during the latter months of pregnancy has at times been due to impaction in the terminal ileum. This may be relieved by gentle irrigation through a catheter passed through the ileostomy.

Let us review some of the larger series of cases of pregnancy after ileostomy, colectomy, and abdominoperineal resection. Scudmore and co-workers [3] report seven pregnancies in five women, with one early abortion (14%) and six live births (86%). In this group some mild complications with the ileac stoma were encountered. Two patients had partial intestinal obstruction which responded to medical management. The six infants were delivered per vaginam. The episiotomy in three instances healed slowly.

Bacon [2] reports seven pregnancies in seven women after ileostomy and total colectomy, all of whom were delivered per vaginam at term without complications. He pleads for delivery through the vagina instead of by elective cesarean section simply because the rectum had been removed.

A colleague of ours, Dr. Clarence Dennis of Brooklyn, N. Y., has written us that he has had eight pregnancies in seven women after total colectomy. All of them were carried to full term and seven of the eight infants were delivered by elective cesarean section. A section had been planned for the eighth patient, but she surprised her obstetrician by a normal delivery with no complications. We cannot agree with his choice of delivery by section unless it is dictated by other factors. In agreement with the method of delivery by Dennis, however, Hull and Magee [4] state that after removal of the rectum the perineum is fixed and inelastic, thus making vaginal delivery dangerous, if not impossible. Along with Bacon [2] and Scudmore and co-workers [3] we have found no such difficulty.

To the above 22 pregnancies with 21 term deliveries after ileostomy and colectomy we should like to add our series which includes 13 pregnancies in seven women with the following outcome: 10 term pregnancies (77%) and 3 early spontaneous abortions (23%). Of these 10 term pregnancies, 9 (90%) patients were delivered per vaginam. One (10%) was delivered by cesarean section. By including our 10 patients there is a total of 31 term pregnancies, all of which terminated in live births, with no maternal mortality. We have had no difficulty with the perineum at delivery. An adequate episiotomy can be made with safety in the absence of the rectum. One of our patients, a multipara, required no episiotomy.

Report of Cases

Case 1.—A patient developed symptoms of ulcerative colitis at the age of 12. By the age of 20 she had undergone two operations for rectoperineal fistulas. Fifteen years after the onset of her disease an ileostomy and colectomy were performed, with a rapid recovery. Two years later she became pregnant; her weight increased to 155 lb. (70.3 kg.), she delivered normally after a 12-hour labor. She again became pregnant after three months. This pregnancy also ended uneventfully. Since that time she has had two early spontaneous abortions without complications. She is well and is an advocate of this operation before pregnancy.

Case 2.—This patient had her first symptoms of acute ulcerative colitis at the age of 23. Two months later she entered the hospital and remained four and one-half months on medical management. One and one-half years later an ileostomy and colectomy were performed. Ten months later she became pregnant. During pregnancy she remained well and comfortable except for an occasional cramping sensation near the ileostomy stoma. She gained 25 lb. (11.3 kg.) and her hemoglobin level rose from 10 to 13 Gm. per 100 cc. She was delivered by outlet forceps after an 11-hour labor. The postpartum course was uneventful. Although her condition remained good, she had a vaginal Pomeroy sterilization six years later.

Case 3.—This patient was unmarried. Ulcerative colitis was diagnosed at age 13. Four years later an ileostomy was performed, and two years later the last stage of the colostomy was completed. Ten years after treatment for the colitis, she was hospitalized for pulmonary tuberculosis, and while still under pulmonary therapy she became pregnant. She gained 19 lb. (8.6 kg.) in the pregnancy. In the seventh month of gestation she had evidence of a partial bowel obstruction which responded to conservative management. She was delivered by low forceps at term after a 14-hour spontaneous labor. There were no postpartum complications.

Case 4.—This woman, aged 31, had her first symptoms of ulcerative colitis at age 16. Two years later she weighed 80 lb. (36.3 kg.) and entered the hospital for colectomy and ileostomy. She was free of complications from that time on. Seven years after surgery she delivered a 6-lb. (2,721 Gm.) infant in her 38th week after a 13-hour labor. A central episiotomy was used. Two years later she had another uneventful pregnancy and delivered normally a 6-lb. infant in breech presentation after a seven-hour labor. Her hemoglobin level ranged between 11.5 and 12 Gm. per 100 cc. with each pregnancy.

Case 5.—This woman had one pregnancy prior to the onset of her ulcerative colitis. She had one pregnancy and a therapeutic abortion after the onset of her disease. There was almost continual bleeding and the development of several fistulas in the four years prior to her colectomy and ileostomy. Five years after this operation she became pregnant and progressed satisfactorily until the seventh month, at which time she developed a partial intestinal obstruction which responded to conservative treatment. She delivered two weeks before term a 6-lb. 15-oz. (3,147 Gm.) baby after a five-hour labor. Her hemoglobin level was 11 Gm. per 100 cc. Four years later she delivered an 8-lb. 3-oz. (3,714 Gm.) infant normally after a four-hour labor. She has been well since then.

Case 6.—This patient, aged 34, developed symptoms of ulcerative colitis at age 26 after the birth of her first child. Eight months after the onset of her disease an ileostomy was performed. The colon continued to be inflamed and 11 months later a hemicolectomy was performed. Several months later she had a spontaneous abortion. The remaining colon was removed one and one-half years later. Her fourth pregnancy, or the second since the colectomy, occurred six years after her primary surgery. She had an uneventful pregnancy and delivered a 7-lb. (3,175 Gm.) infant normally after a five-hour labor. Her hemoglobin level on admission was 14 Gm. per 100 cc. One month later she developed an abdominal wall abscess adjacent to the ileostomy which required incision and drainage. Recovery was rapid and complete.

Case 7.—This woman, aged 32, first developed ulcerative colitis at age 14. Six years later she had an ileostomy. The remaining colon was removed in two stages the following year. Her only complaint thereafter was an occasional enteritis. Ten years after the ileostomy she became pregnant. In the sixth month she developed an intussusception of the terminal ileum which had to be revised. The pregnancy was marked by nausea above the usual amount and an occasional episode of diarrhea. She was delivered at term by a low fundal cesarean section after a 22-hour trial of labor with the breech presenting. Seventy-two hours after delivery she developed a volvulus with gangrene of the terminal ileum which was resected and revised. She was discharged improved and remained that way for one year when she developed acute abdominal pain with a transient partial obstruction, which responded to conservative therapy.

Conclusions

It is relatively safe for the young woman with an ileostomy and colectomy to go through pregnancy. Early and adequate prenatal care is of the utmost importance. The care of each patient should be individualized in the joint decision of the surgeon, the gastroenterologist, and the obstetrician.

Seven women had 10 live births in 10 term pregnancies. Three pregnancies terminated in early spontaneous abortions. There was no maternal mortality. In 9 of the 10 term pregnancies the patient was delivered per vaginam; one was delivered by cesarean section. No difficulty with the perineum was encountered at vaginal delivery.

Three patients had evidence of partial small intestinal obstruction. Each of them responded to medical management. One patient developed an intussusception at six months gestation and required a revision of the ileostomy. This patient was delivered by cesarean section, after which she developed obstruction requiring resection of the terminal ileum.

Pregnancy in Patients with Ileostomy and Colectomy

Case	Age	Wt. of Baby, Gm.	Gestation	Duration of Labor, Hr.	Type of Delivery	Hemoglobin Level, Gm./100 Cc.	Complications
1	31	3,430	Term	10	Normal	13	None
	32	3,402	Term	8	Normal	12	None
2	26	3,288	Term	11	Outlet forceps	13	None
3	27	3,175	Term	14	Low forceps	12	Obstruction, 7 mo.; bled from ileostomy
4	26	2,721	38 wk.	13	Normal	12	None
	31	2,721	Term	7	Breech	11.8	None
5	34	3,147	38 wk.	5	Normal	11	Obstruction, 7 mo.
	38	3,714	Term	4	Normal	12	None
6	34	3,232	Term	5	Normal	14	Abdominal wall abscess
7	29	3,005	Term	22	Cesarean section	13.8	Volvulus, 7 mo.; postpartum obstruction

We feel that the young woman with ileostomy and colectomy may lead a relatively normal life and may undergo pregnancy with the expectation of a normal delivery in most instances.

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MEDICAL-LEGAL ASPECTS OF INJURIES TO THE NECK

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It is fallacious to speak of all injuries to the neck in automobile accidents as whiplash injuries and to classify all patients with true whiplash injuries into one group. There is a gamut of injuries from the inconsequential to the fatal, and injuries to the neck vary not only in degree but also in kind. Confusion and injustice can be avoided only if all parties, including lawyers and physicians, are objective, explicit, and honest in handling cases of personal injury. The physician who is consulted should be thorough in his examination, keep good records, be prepared to translate his medical phrases into practical terms, and bring charts, models, or other visual aids with him to court for the information of judge and jury. A just settlement depends on the mutual respect and cooperation of the medical and legal professions.

The term "whiplash injury" was fathered by the medical profession and popularized in an article by Gay and Abbott which appeared in The Journal in 1953.[1] Since 1954, the term "whiplash injury" has become the darling of the plaintiff's attorneys and the bane of the defendant's atorneys. A persuasive lawyer with a modicum of histrionic ability can almost make a jury follow the course of his client's head and neck as it snaps backward two or three feet and is then propelled forward. Today, because of the confusion engendered by the faulty terminology, most physicians would like to rename the monster they created. One well-known authority has suggested "necklash injury." That substitution would still lead to confusion, inasmuch as many of the injuries sustained by the bony elements of the neck are not caused by any real lashing movement. It might be more useful to return to our physical findings as a source of our descriptive terminology. Why not call a sprain a sprain, a concussion a concussion, and a fracture exactly what is it?

Where equally competent and reputable physicians draw conclusions that are almost completely contradictory and opposite, it is no wonder that attorneys, simply by reading the medical literature, can find any variety of opinion that will best serve their purpose. In a law journal recently, an editorial which introduced a symposium on whiplash injury stated:

> It is amazing how attorneys can support their theory of the case, whether for the plaintiff or for the defense, by showing adverse doctors specific supporting medical literature on whiplash from authoritative journals—like The Journal of the American Medical Association or journals of the specialties of neurosurgery or orthopedics.
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> When it is a matter of convincing a doctor or lawyer on medical causation or evaluation of disability, current pertinent medical articles or books pertaining to whiplash will invariably impress them with the reliability of the medical basis for one's theories.

Some recently reported cases have shown how effectively articles on whiplash from The Journal can be used in effective cross-examination of defense medical witnesses. It may be proper for plaintiff's counsel to test the knowledge and accuracy of defendent's physician on cross-examination by reading pertinent extracts from The Journal pertaining to whiplash and to ask whether he disagrees with what has been read. Confronted with the authority of The Journal, most physicians on the witness stand would be inclined to agree with what had been written therein. This, of course, is influential in reducing the weight of adverse medical testimony even when a physician disagrees with what has been stated in The Journal. Attorneys may effectively demonstrate to the fact finders (the jury) *that the physician is disagreeing with a widely* accepted authority. However, there are certain dangers in using articles or textbooks to discredit medical witnesses, if the attorney improperly quotes pertinent and favorable sections from them to the jury on summation. This is especially so when an attorney confronts an adverse medical witness with a dozen or more accepted medical authorities which he refuses to admit as authoritative and/or disagrees with entirely. Then, in the closing argument, the attorney emphasizes to the jury the fact that the adverse physician maintains his own opinion in the face of a dozen other widely accepted medical authorities whose opinions were contrary to his own. This may contribute to prejudicial error.

Attorneys will find, in reading the medical literature, information which will best support their theories for defense or prosecution in present or future whiplash cases. It is imperative to bear in mind that generalized conclusions drawn from one physician's study of 100 or more cases are not of necessity representative of the conclusions that might be drawn if 1,000 or more, treated by physicians from all sections of the United States, were evaluated. Thus, the reports by Gay and Abbott,[1] Gotten,[2] and others simply represent their findings, and the many variables that come into play in the possible

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causation of neck injuries cannot be taken into account. Among these variables are preexisting arthritis or disease, the normal or abnormal posture of the patient, the age, the force with which the vehicle was struck, and the position of the patient inside the vehicle. A statistical study—which must include more than 1,000 cases, would be more truly representative. The editor of the law journal concludes:

> From the point of view of medical terminology and whiplash, there are advantages in using one of several accepted medical terms for whiplash disability. Certain plaintiff's medical terms in the form of "whiplash injury" or "disc injury" in the neck, will give an implication of a greater amount of disability. On the other hand, medical terms like "neck strain" or "cervical syndrome" could effectively be used by the defense and imply less disability. Since all of these terms are accepted medical diagnosis today, it is important that one case should be prosecuted or defended on the basis of such specific diagnosis—depending on whether one is representing the plaintiff or defendant.

It is difficult to deny that confusion does arise whenever neck injuries produced by a whiplash-like mechanism terminate in a court of law. A reevaluation of the symptom complex of injuries to the neck may, therefore, serve a useful purpose if only to place the physician where he belongs, namely, as an impartial agent whose sole interest is providing for the welfare of his patient instead of being an advocate for plaintiff or defendant.

The National Safety Council has estimated that 15% of all automobile accidents occur when a car is struck from behind, usually when the forward vehicle is stopped. An indeterminate number of vehicles are struck from the side and front. Such forces are likely to be responsible for a more disabling type of injury than is usually found after the flexion or extension movement of the head. Bechtol used dummies to demonstrate that accidents and crashes at 10 miles per hour were responsible for more damage than were crashes at higher speeds.

Mechanics of the Injury and Anatomy

It has been recognized that forced motion of the head and neck in one direction with the body as a base is often followed by a sharp motion in the opposite direction. The various forces that may be transmitted to the neck are compression, distention, bending, shearing, and torsion. If the forward motion of the body within the carrier suddenly stops, the head continues forward, but if the body and the carrier are suddenly propelled forward, as in rear-end collisions or in catapult launchings, the head is whipped backward. Then, in rebound, it is driven forward, completing the first full so-called lash movement. If the head and neck are turned at the time of impact or if the impact comes from the side, severe torsional forces may then be transmitted to the neck and the structures within.

The mechanical structures of the neck are so constituted that the neck can tilt forward, backward, and sideward and rotate by a gliding motion in the facets. Extremes of motion are limited by the anterior, posterior, and lateral ligaments as well as the capsule and fibrous tissue structures which surround the joints.

The relationship of the covertebral joints to the vertebral artery and the cervical nerve roots must be understood before one can begin to appreciate and believe the injured patient's complaints and symptoms. The nature of the intervertebral disk, the physical chemical properties, and its newly discovered though meager nerve supply must also be more fully understood. With loss of water content and concomitant loss of height of the disk, there may be an altered mechanical alignment of the cervical spine. There may result abnormal compression force on the posterior ligaments through which the peripheral and autonomic nerves must pass, hence, the not uncommon sensory, motor, and sympathetic nerve manifestations which are often demonstrable by electromyographic studies.[3]

The normal fundamental anatomy of the neck must also be understood if deviations from the normal are to be recognized. The special design of the atlas and the axis permits nodding, rotation, and lateral bending movements of the head. Motions in the other cervical joints consist of forward flexion, extension, lateral bending, and rotation. The last two movements occur together.

The ligaments are lax enough to allow normal movement. Abnormal laxity may give rise to dislocations or allow an abnormal amount of movement to occur, thereby increasing the wear and tear and stress on the joints. Excessive movement of the atlantoaxial joints is controlled by the strong check ligaments. The odontoid process of the axis may be fractured. When such injuries are accompanied by tears of the check ligaments and capsule, posterior dislocation of the atlas can occur. Anterior dislocations may occur when the ligaments and capsule are torn.[4]

The secondary joints or intervertebral disks are narrower in the cervical region. The vertical diameter anteriorly is from two to three times greater than posteriorly. The nucleus pulposus is more anterior than in other disks and is, therefore, less subject to rupture than is the nucleus in the lumbar disk.

The shape and inclination of the primary articular processes and the slight laxity of the ligaments and capsule structures contribute to the range of normal motion. The important joints of Luschka [5] are small synovial articulations measuring 2 by 4 to 3 by 6 mm. They are situated between the five lower cervical vertebrae and lie anteromedial to the mixed nerve root and posteromedial to the vertebral artery, veins, and sympathetic nerve supply. The significance of injuries involving Luschka joints is based on their proximity to the important nerve and vascular structures as well as the ligaments. The lower cervical nerve roots, being relatively fixed in position, may be exposed to trauma or compression, particularly when the neck is flexed at the moment of impact, as when a vehicle is struck from behind. Pain may be referred from nerve roots which, as they leave the bony outlet or foramens, are compressed by inflamed ligaments and capsules, adhesions, and pressure from osteophytes and thickened soft tissues, including a thickened ligamentum flavum.

It is thought that the Luschka joints restrict lateral flexion of the neck and may prevent lateral herniation of the nucleus pulposus. Morton[6] states that nerve symptoms are more frequently caused by Luschka joint exostoses than by osteophytes arising from the apophysial joints. Exostoses from Luschka joints may encroach on the vertebral artery and be partially responsible for the so-called shoulder-hand syndrome. The complications from lateral or oblique flexion forces must not be minimized, since such forces are responsible for injuries to the Luschka joints and to the surrounding sensitive and important soft tissue structures.

An analysis of 75 patients with preexisting degenerative changes in the neck revealed only 7 with a definite diagnosis of herniated disk. It may be that clinical symptoms pertaining to cervical nerve roots are more often due to the arthritic and degenerative changes of the synovial joints of Luschka. It has been suggested that many of the hard protrusions removed by neurosurgeons are spurs and calcareous deposits formed on or near the Luschka joints. This is a field of inquiry which has not been pursued too well.

The joints between the sixth and seventh cervical vertebrae are freely movable; however, the less mobile joints between the fourth and fifth and fifth and sixth vertebrae are more vulnerable to stress and injury. Careful x-ray examination is necessary to localize injuries in this area.

The absence of posterior joints between the head and the atlas and the atlas and the axis leaves the first two spinal nerves without an intervertebral canal. The other five vertebrae do have foramens through which passes a spinal nerve. Whenever the head is turned, there is a gliding motion between the lateral intervertebral joints. Forced motion may subject the roots and the accompanying blood vessels to irritation and injury.

Sympathetic Nervous System

In order to more fully understand the picture of the cervical nerve root irritation, the role of the sympathetic nervous system must be examined and understood. The cervical nerve roots are composed of motor and sensory fibers only. The dorsal and upper two lumbar roots contain specialized communicating elements, which in the case of the upper two dorsal roots serve to join the cervical roots and procede upward to the cervical ganglions. From the cervical ganglions fibers pass to the cervical nerves, the cranial nerves, the heart, the arteries of the head, neck, and arms, and other important structures. Other fibers contact or communicate with small special meningeal nerves before they run back through the intervertebral foramens to supply the dura. The special meningeal nerves also supply a portion of the sensation of the ligaments.

Irritation directly to the sympathetic nerves may give rise to symptoms which are identical with those arising from primary injury or irritation of the cervical roots. Conversely, primary irritation to the roots may secondarily irritate the sympathetic innervation and cause thorough confusion. It is because of this confusion that many learned investigators agree that the explanation of the mechanism of pain in the neck and back is still incomplete.

The soft tissues that surround the bony components of the neck are more frequently injured than are the vertebrae. The muscles attached to the upper two vertebral bodies, as well as the blood vessels that supply them, may be contused, stretched, or torn. Hematomas may form and give rise to pain extending from the second vertebra to the undersurface of the scalp. The sternomastoid muscle is frequently injured by the oblique injury. Pain in the angle of the jaw near the ear is not infrequent. The patient may also complain of a painful neuralgia which is often overlooked.

As severe injuries to the muscles in the surrounding fascia heal, small neuromas or fibrocytic nodules may form and create painful "trigger points." Motion of the neck may thus be limited. Prolonged supportive measures may be responsible for the development of fibrosis. Prolonged and unrelieved muscle spasm may lead to the same complications. When to begin movement and how to relieve spasm calls for sound medical thinking and judgment. Muscle relaxants, traction, and other physiotherapeutic measures are often used.

Eye, Ear, and Balance

Eye.—Pupils of the eyes and the associated structures can provide many valuable clues in the diagnosis of residual trauma from injuries about the neck. Interruption or dysfunction of the sympathetic pathways to the head may produce Horner's syndrome: (1) dropping of upper eyelid, (2) constriction of pupil, and (3) loss of ability to tear or water. Patients with so-called whiplash injuries frequently complain of blurred vision or difficulty with focusing. Dilated pupils and a flattened lens may result from sympathetic stimulation. The study of pupillary oscillations with the slit lamp may well become a routine office procedure when the realization of the part that eye changes play in evaluating neck injuries becomes more apparent.

Ear.—Cervical trauma rarely produces symptoms of otological significance other than pain to the ear. The patient's complaints of dizziness of a transitory nature, loss of hearing, and pain require a careful ear, nose, and throat examination.

Balance.—The tonic neck reflexes act in adjusting the tone of postural muscles throughout the body. A change in the position of the head brought about by even a slight asymmetrical tension in the head or neck may make tasks requiring accuracy very difficult. Injuries to nerves, muscles, and tendons of the neck can seriously decrease the quality of performance of highly skilled industrial workers.

Symptoms

Injury.—Collision from behind usually thrusts the head acutely backward. The neck muscles attempt to compensate and right the position of the head; instead, overcompensation may develop, and the neck is forced forward. It is the latter movement that is thought to produce the greatest damage through the mechanism of deceleration.

Concussion to the spinal cord and the base of the brain may develop during the acceleration extension movement and, more often, during the deceleration oscillation of the head. The capsular tissues and the accessory ligaments may stretch or tear. Swelling within these structures from hemorrhage may compress the nerve roots. Lateral or rotational forces, as when a vehicle is struck from the side, may alter the size of the intervertebral foramens and further irritate a cervical nerve root. Extensive tears of the ligaments and capsular structures may allow anterior or posterior dislocations of the vertebral bodies. Such injuries to the soft tissues are, of course, not visualized by x-rays.

Individuals past 30 years of age and those with a history of trauma or disease of the bony and soft tissue elements of the neck often may show evidence of degenerative changes about the articular processes of the lateral joints of Luschka or on the forward lips of the vertebral bodies. These spurs or osteophytes diminish the normal flexibility and mobility of the ligaments and joints and tend to give the neck a diminished resistance to the shock of severe forces which have been applied to the area. Spurs may be broken loose, and, when such an injury is so demonstrated by the x-ray examination, the examiner should be alerted to the presence of injuries to the contiguous ligaments and soft structures. What is seen by x-ray then may be only the minor manifestations of a more serious injury to the soft tissues. The more troublesome complications often go unheeded, since the x-rays are capable of showing only bone shadows clearly.

Symptoms may be divided into six categories: (1) transient sprain, (2) cerebral concussion, (3) cervical radiculitis and soft tissue injuries, (4) subluxation, (5) fractures with or without subluxation, (6) disk involvement, and (7) psychoneurotic changes.

Transient Sprain.—When a vehicle is struck from behind and the occupants have been forewarned, they can often brace themselves and avoid the severe muscular forces that are exerted on relaxed tissues. Paradoxically, forces from cars which strike at excessive speeds may do less damage than those from cars which strike at 10 miles per hour or less. The greater impact may dislodge the occupants as well as the seats, thus dissipating some of the force applied to the neck. The patient may complain of transient stiffness in the cervical muscles and may exhibit, on x-ray, a temporary loss of the normal cervical curve. Response to rest, heat, and sedation is usually rapid.

Cerebral Concussion.—The deceleration injury may, in a large number of cases (22-30%), produce concussion to the frontal and occipital areas of the brain. Torsional forces may, likewise, involve the brain stem, the area of the brain just above the spinal cord. The symptoms range from loss of consciousness for a varied period to confusion, dizziness or vertigo, headache, inability to concentrate, and disorientation. Some of the symptoms have been found to last for several years.

Cervical Radiculitis and Soft Tissue Injuries.—Symptoms of pain along the course of specific nerve roots or into a particular muscle area are common. More than one-third of my patients could be classified as having such findings and complaints. The most common complaint is of pain and rigidity in the muscles on one or both sides of the neck posteriorly. When the injury has been fairly severe, the patient may complain of swelling or edema due to irritation and injury to the underlying ligaments and muscles in front of the cervical vertebrae. This finding is transitory and can only be elicited by the physician who sees the patient immediately or soon after the accident occurs. There may be change in the reflexes of the arms (biceps and triceps), and pain may radiate into the occipital region, shoulder, arms, chest, hands, and jaw. Pupils may be dilated, and transitory vertigo is not uncommon.

Injuries to the neck do not always give immediate symptoms. Often the onset of pain may occur several days after the injury or, in stoic persons, may not come to the attention of any physician for several weeks. Slight pain on motion of the neck with progressive increase of the pain and secondary splinting, or rigidity of the muscles, is perhaps the most common finding in this type of injury. Too often, the patient who first complains of pain several days after the accident is accused of malingering. It is not uncommon for patients who have sustained fractures of the vertebrae to complain of little or no pain for periods of several days to several months.

Objective findings or symptoms which persist for a month or more suggest the possibility of a chronic course which may last for as long as two or three years. Persistent rigidity in the muscle groups may lead to irreversible changes in the make-up of the muscles and the ligaments. Relatively flexible tissues may be converted into flexible, almost avascular scar tissue, with a lower resistance to reinjury. It is for this reason that immobilization of the muscles of the neck for prolonged periods is often contraindicated, since this type of overtreatment may, in itself, lead to the same irreversible changes that develop after serious injuries.

Subluxation.—Ruptures of the ligaments and capsular tissues may allow forward or backward dislocations of the vertebrae, depending on which ligament is torn and how severe the injury may be. Such dislocations may reduce themselves spontaneously and may not be noted unless special x-ray techniques are used. These include careful lateral x-rays taken with the neck in flexion and extension. Muscle splinting and rigidity may have to be released by the use of orally given muscle relaxants or by the injection of local anesthetic agents. Extreme care must be taken to avoid unguarded excursion of the neck and possible subsequent injury to the cord.

Posterior dislocation may occur without evidence of accompanying fracture. This displacement usually follows a severe hyperextension force. Anterior dislocations may occur when the neck is in flexion, particularly at the time of impact. Directly after such an injury (dislocation) there may be spontaneous correction and maintenance of correction by muscle splinting or spasm. Infrequently, with severe dislocations there may be cord involvement either by contusion and swelling with transient paresis or paralysis or by severance of the cord and subsequent irreversible paraplegia or quadriplegia.

Fractures.—Compression forces, such as in lash injuries, may fracture or crush to a varying degree the vertebral bodies, particularly the fifth and sixth cervical vertebrae, which are relatively immobile. Fractures of the odontoid process are rare and are often overlooked. Special x-ray techniques may have to be used to identify the fractures.

Fractures of the spinous processes are also rare. I have only seen one such case resulting from a lash injury. Dislocations can accompany fractures of the cervical arches. Torsional lash stresses are thought to be responsible for this more serious type of injury.

Cervical Disk Involvement.—The use of the term "cervical disk" unfortunately has been taken to indicate that a rupture has taken place and is responsible for irritation of nerves which are thought to, but do not, lie immediately posterior to the disks. The disks have a high water content, and it is the liquidity of the mass that makes up the disk which allows it to absorb some of the shock of weight-bearing of falls which would otherwise be transmitted directly to the spinal cord and brain and cause concussion and permanent injury. The nucleus pulposus is embedded forward of the middle of the disk in the cervical area. Surrounding the whole disk is the tough ligamentous structure, the annulus fibrosus, which may be torn or ruptured during the extension-flexion movement of the neck

Immediate symptoms of pressure on the cord o the nerve roots are most unusual from lash type of injury. Gay and Abbott [1] have estimated that 20 of their patients develop full-blown cases of th ruptured disk syndrome 18 to 24 months after th initial injury. It is my belief, and other authoritie agree, that symptoms from the so-called rupture cervical disk syndrome are more often caused b injuries to the lateral intervertebral joints whic are in contiguity with important nerves and arteries. Where there is a severe tear in the annulus an posterior longitudinal ligament, ruptures of th cervical disk may be more likely to compress th cord rather than the cervical nerve roots. The attorney who examines the expert witness must determine the witness's awareness of this relativel new knowledge of the anatomy and pathology o injuries to the intervertebral joints of Luschka.

Psychoneurosis.—Emotional upsets may be imme diate or delayed. Stoic persons may show little o no change. People, though, are different physicall and emotionally, and resistance to disease varies a does response to injury. Many patients develop fear reaction over the knowledge of possible com plications from injury to the spinal cord and brai Hostility toward the driver of the other car is com mon and is often the basis of an emotional reactio Frustration from an obvious or imagined lack of i terest by the physician and accusation of malinge ing may produce a state of tension which protrac the period of pain and may lead to psychoneurot reactions.

It is necessary for lawyers, as well as ma equally badly informed physicians, not to confu nervous tension with intentional malingering. Go ten, a neurosurgeon, in an often quoted pap which appeared in THE JOURNAL, concluded th 54-85% of traumatized patients showed total moderate improvement after financial settlemen The injury, according to Gotten, has been used b the patient as a lever for personal gain. Gotten data are somewhat untenable. Most patients d show some or marked improvement after tw years (two years represents the average time before litigation was completed in Gotten's cases It is impossible for me to believe that 85% of an group could be conscious or unconscious malinge ers. Gotten's data were evaluated by medical students, who cannot be expected to understand th complexities of the whole already confused pictur of neck injuries. Generalizations are dangerou and inaccurate. Every case must be judged on it own merits.

Diagnosis

Preexisting Conditions.—If the injury occurs to a patient who has had preexisting osteoarthritis, spurs or osteophytes may be broken and cause irritation and ligaments which are rendered inflexible by old scars may rupture more easily. Disks which have undergone previous degeneration and have become dehydrated may suffer further injury, and the process of degeneration may be speeded. Patients who have had long debilitating illnesses may be subject to dislocations because of increased laxity in muscles and ligaments which surround the vertebrae. It must be emphasized that distress or physical signs need not have been observed prior to the neck injury despite x-ray evidence of degenerative processes which must have been present for a long time.

Congenital anomalies, such as congenital fusion of several vertebrae (usually the second and third cervical vertebrae), may be responsible for throwing undue stress on the vertebrae above and below. Arteriosclerosis, particularly of the vertebral artery, may make this artery more vulnerable to compression. Sclerotic vessels are subject to tearing and may be responsible for hemorrhages, swelling, and secondary irritation to contiguous structures.

Making the Diagnosis.—A careful history and examination is of utmost importance. All injuries are sources of potential litigation. The physician must realize that his duty does not end with examination and treatment of the patient. Accurate records must be kept and careful physical examinations must be done. The eyes, ears, throat, neck, low part of the back, and extremities must be examined. The neurological changes, if any, should be noted on special charts, which should be available.

Electromyographic studies may help localize the site of injury, but the method is still subject to many sources of error in application and interpretation. These studies can furnish information about stages of nerve degeneration and signs of nerve regeneration. Often, signs of nerve regeneration may be demonstrated two months before voluntary movement in a muscle occurs. The electromyogram will not show whether an affected nerve will proceed to complete degeneration.

A form on which a great deal of information can be noted may be used. When the examining physician is unable or unwilling to examine the whole body, particularly the eyes, ears, and throat, or he finds the examination calls for skills and experience he does not possess, he should refer the patient to one or several who can conduct the necessary thorough examination.

The x-ray examination should include routine anteroposterior and oblique films of the neck. Special views to visualize the odontoid and to determine the presence of dislocations are also needed. When symptoms or complaints persist despite previous negative x-ray findings, special views devised by Abel have been found to be most helpful. Abel reported the finding of fractures in a large number of patients whose routine x-rays were interpreted as showing normal findings. Some radiologists, however, question Abel's findings and interpretation of his films and have, within the judicial process, cast some doubt on the value of a statement of positive findings based on his suggested technique. Until the radiologists resolve this difference of opinion, there will remain some understandable confusion in the minds of the lawyers, doctors, and patients.

A persistent loss of the normal cervical curve suggests muscle spasm secondary to an underlying irritation (injury or infection). If x-rays of the neck have been taken for one reason or another prior to the accident, the comparative films can be of great value. Evidence of a normal curvature lost after an accident certainly points to the accident as the most likely causal factor.

Myelographic studies may be used in cases in which accurate diagnosis is difficult and symptoms are conflicting. Supposedly, the use of radiopaque material is perfectly safe, particularly in the lumbar spine. Davis[7] and other authorities admit that myelography is a valuable aid in the diagnosis of intraspinal lesions, but they have reported complications, including persistent headache, nerve irritation, arachnoiditis, stiff neck, leg cramps, and backache. The contrast medium should be removed, but often a small amount remains and may be the cause of these difficulties. Admittedly, these difficulties are rare, but they do occur and must be taken into account in the evaluation of a patient's persistent complaints.

Therapy

Prevention is, of course, the best therapy. Better engineering in cars should include neck extension to the seat back, shock absorbers on the bumpers, and waist and shoulder belts. Driver education and better medical examination for prospective drivers would help eliminate the physically incompetent driver. The danger from the use of certain drugs, including tranquilizers, antihistamines, and barbiturates, may be as important as the elimination of alcohol from the diet of the average driver.

Patients who have persistent symptoms and complaints should be evaluated by a team of physicians. Ideally, such an examination should be done early and repeated after various forms of treatment have been tried. Patients whose complaints and symptoms persist for two months or longer usually can be expected to have a more protracted period of convalescence and inability to return to normal activities. The average period of disability in such a case has been from 18 to 36 months. The optimum time for settlement is 18 months in cases with severe injuries. Patients whose settlements are delayed longer often manifest neurotic tendencies which make subsequent settlements extremely difficult. Again, it must be reiterated that neurotic manifestations can and do develop in patients who have suffered real and serious injuries.

The treatment should be individualized and should begin immediately after the completion of the examination. Hospitalization for one to two days or longer is useful for disturbed patients who have just been subjected to a severe crash injury. Complaints that are not noticed immediately after injury may come to light in 24 to 48 hours or later.

The patient is advised to rest on a firm bed for at least 24 hours. Analgesics and sedatives may be given at regular intervals. Where neck muscles are painful, a Thomas collar or other type of cotton or plastic collar is applied to place the muscles at rest. Traction of an intermittent type may be used, with weight from 7 to 15 lb. Wet or dry heat can be applied to the neck, and painful muscles may be injected and orally given muscle relaxants used. If the physician honestly feels encouraged, he should reassure his patient and educate him to understand the process of injury, healing, and convalescence.

The outlined treatment, then, should include (1) reassurance, (2) heat, (3) massage, (4) traction, (5) injection and orally given relaxants, (6) correction of faulty body mechanics, (7) immobilization, (8) drugs, (9) psychotherapy, (10) consultation or reference to specialists, where necessary, and (11) operative intervention, only when the indications are clear.

Comment

Conclusions of Plaintiffs' Attorneys.—Plaintiffs' attorneys, after studying the inadequate statistics, have made the following conclusions. Headache is complained of in about 55% of the cases. In 90%, pain is present in the neck on one or both sides, and in 25% there is pain in the chest. Stiffness in the neck is noted in about 80% of the patients; whiplash victims ordinarily are unable to comb their hair, button their shirts, or get their hands in their hip pockets. Blurring of vision is seen in victims with recent injury; there may be a loss of balance in about 15% of the cases. Numbness and tingling of the fingers is an annoying complication; there may even be blackouts indicating an injury high in the neck. Weakness of the arm is a frequent complaint, and in 15% weakness of the grip is noted. The reflexes, which are also valuable objective evidence, may, nevertheless, be entirely normal. Another valuable objective piece of evidence is definite difference in the blood pressure reading of each arm; pressure may be as much as 10 to 20 mm. Hg higher on the involved side. Dilation of the pupil is a valuable objective sign which is frequently found immediately after a whiplash injury.

Painful areas need not always follow consistent nerve patterns, because the final distribution of a cervical nerve may not be confined to its corresponding origin in the neck. There may be an overlapping of spinal nerve distribution to the arm, hand, and forearm. Hadley[8] states that one of the most important permanent deformities after whiplash is angulation of the neck. This may result in a permanently stiff deformed neck. Hadley confirmed these clinical observations with autopsy examinations on cadavers. Degeneration of the cervical intervertebral disks after whiplash injury is not uncommon and may appear a year or two after the injury. Twenty per cent of patients who have fairly severe injuries develop ruptured disk syndromes within 18 to 24 months after injury. It is important to note that acute symptoms may be initiated or precipitated by a new injury or by some trivial nonlegal activity, such as stooping over, turning over in bed, or reaching backward.

Conclusions of Defendants' Attorneys.—The defendants' attorneys have, from equally insufficient data, made the following conclusions. The greatest problem confronting the defense in these cases in the fact that most doctors are inclined to accept, at face value, the plaintiff's complaint. They give full credence to all he says about his pain and his complaints without taking into consideration the motives or the possibility that he has a damage suit pending. Where there is an allegation of irritation of the cervical nerve roots, the defense should bear in mind that the greatest percentage of these cases occur in persons in the third or fourth decade of life. A complaint of cervical nerve root irritation in plaintiffs under the age of 30 years should be regarded with suspicion by the defense. Where there is an allegation of severe whiplash injury with the additional allegation of complication of pain and disability caused by irritation of the nerve roots, there are certain other intrinsic nontraumatic medical conditions which could be the sole or substantial cause of the disability. Patients' physicians should be asked the following questions: Did you ascertain whether the patient's neck pain could be reflexly referred from visceral structures, such as disease of the heart or lungs? Did you determine whether the pain and disability could have resulted from an irritation of a nerve or branch of a nerve other than those arising from the neck? Did you determine whether the pain or disability could have been caused by some other focus within or without the spinal cord? Did you determine whether the pain could have resulted from a possible brain lesion, tumor, or small cerebellar hemorrhage? Did you determine whether the patient's pain and disability about the neck could have been substantially due to psychogenic or psychosomatic origins which predated the injury? In a large proportion of the cases, the so-called whiplash symptoms are only incidental. Certain postures and occupational attitudes can cause chronic hyperextension of the neck similar to that seen in whiplash injuries. Patients who are under general anesthetic and who have been handled unnecessarily or roughly may have an injury to the ligaments and muscles about the neck;

this history must be looked into. Congenital anomalies, per se, can cause narrowing of the canals in which the nerves are found. Such degenerative changes may be a part of the aging process and have nothing to do with the injury. No result of whiplash injury is possible in the lower part of the back because the lower part of the back does not have the extreme mobility that the neck has. More than 88% of patients with so-called whiplash injury get well after settlement. Fifty-four per cent have no residual complaints, and 34% have only minor symptoms not requiring any medical treatment. There is some evidence that whiplash injury may be used by patients as a convenient lever for personal gains. Rupture of the cervical disk after whiplash is almost unknown.

The accusation that lawyers can buy any type of medical opinion that they desire is unjust and untrue. In retrospect, it is now obvious that order can be restored from the chaos that exists only through the good offices of medical organizations. The American Academy of Orthopedic Surgeons will, in 1960, present a symposium on whiplash injuries in which every aspect of the anatomy, pathology, diagnosis, and treatment will be discussed. A review of the information that has been accumulated to date and a study of cases treated by dozens of surgeons from all parts of the United States will be useful.

Expert Witnesses.—The physicians best suited to evaluate a lash injury include orthopedic surgeon, neurosurgeon, neuropsychiatrist, ear, eye, nose, and throat specialist, and, where the orthopedist is unable to supervise the physiotherapy, a physiatrist or a physician who specializes in physical medicine. A competent radiologist is often needed to interpret the complex x-rays. The physician should understand that his reports will probably be used in litigation and that he will be asked to translate the medical terminology into terms any layman could understand. Visual aids, such as charts, models, or drawings, should be brought to court so as to properly inform the judge and jury.

Summary

The term "whiplash injury" should be replaced by more accurate and descriptive terminology. The anatomy of the cervical area is complex, and it must be understood before the complaints of the client or patient can be evaluated. Injuries to the neck are common and may be severe. Cursory examinations of the patient may lead to misdiagnosis and protracted symptoms. Neurosis and medical-legal complications may develop in badly handled cases. Evaluation in prolonged cases requires medical teamwork. Preexisting conditions may aggravate the symptoms of whiplash injury. Such preexisting conditions may have been entirely without symptoms and unknown to the patient. Most of the injuries are minor sprains and respond to treatment quickly. Those cases with delayed convalescence offer a more guarded prognosis, and accurate evaluation in these cannot be made in less than 12 to 18 months.

Treatment should be begun early. Reassurance and psychotherapy, not necessarily by a psychiatrist, are important. Pain from tension heightened by neurosis should not be confused with malingering. Physicians should keep accurate records and refer patients to specialists when necessary. The treatment of an injured patient does not always end in the physician's office. The just settlement, which often depends on his testimony, may be more therapeutic than medication.

Cervical disk ruptures are an uncommon immediate complication of neck injuries. Injuries to the lateral intervertebral joints of Luschka are perhaps the most common complications and cause of cervical radiculitis. Extremes of opinions should be avoided. Those who imply that as many as 84% of these patients are malingering are as wrong as those who state that all neck injuries are serious and compensation should be given on the basis of total permanent disabilities.

Each case should be carefully examined, reexamined, evaluated, and reevaluated on its individual merits. It is fallacious to classify all patients with lash injuries into one group—particularly since the findings may run the gamut from inconsequential sprain to fracture dislocation and cord damage. Physicians and lawyers who handle personal injury cases must begin to think in terms of symptoms, such as concussion, sprain, radiculitis, dislocation, and fracture. Finally, the dishonest or incompetent lawyer who deliberately exaggerates his client's claims is often supported by equally dishonest or incompetent medical experts. Fortunately, the vast majority of the members of both professions are upright, honest citizens. Only through mutual respect and cooperation can the client patient expect a just settlement.

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PROBLEMS IN REHABILITATION OF THE HEMIPLEGIC PATIENT

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The new philosophy of the treatment of hemiplegia emphasizes attention to the portions of the body that remain functional. But it must be recognized that brain damage limits the goals of rehabilitation. Among the 122 patients here studied, there were 23 judged to be physically able to return to work, but of the 11 with right-sided hemiplegia, 6 are now employed, while of the 12 with left-sided hemiplegia, only 2 are now employed. Vocational rehabilitation was thus more likely in patients with involvement of the dominant hemisphere. Much can be done for the patient during the first 7 to 10 days of flaccidity, during the ensuing period of spasticity, and finally during the period of retraining in ambulation and self-care. By early and persistent use of what is available, especially in the choice of assistive devices, many hemiplegic patients can be made self-sufficient, thus relieving their families and friends of much of the burden of their care.

In recent years the attitude of the medical profession toward the hemiplegic patient has changed from one of hopelessness and rejection to one of optimism and enthusiasm. This is the result of the development of advanced rehabilitation techniques applicable to the hemiplegic patient. The previously prevailing philosophy contended that, since hemiplegia is the result of brain damage and there is no regeneration within the central nervous system, recovery is impossible and no treatment is indicated; therefore these unfortunate people were given diagnoses and treatment was instituted to save life. But when the physician was reasonably sure that death would not ensue, the patient was discharged to his home or a nursing home where he existed as a bed-patient, occasionally hobbling about the room or sitting in a chair but requiring care from relatives, friends, or professional personnel in order to stay alive. This course of treatment was the natural result of medical training which emphasized the patient's disability and disease without consideration for his remaining abilities.

This has been replaced by a new philosophy. Attention is now paid not only to the disabled area and the crippling disease but also to the portions of the body which remain functional and with which the patient may be able to carry on fairly normal activities, not only living but enjoying life. For example, when the weatherman states that tomorrow will be partly cloudy, he could as well say that it will be partly clear. Emphasis can be transferred from the cloudy to the sunny, from pessimism to optimism. In rehabilitation the emphasis is transferred from disability to ability.

However, as is usual with new things in medicine, the pendulum tends to swing too far, and this has been the case with our attitude toward hemiplegia. Certainly we should be optimistic and enthusiastic about the improvement in the treatment of these patients, but, at the same time, we should realize that there are certain very serious problems which must be taken into consideration in the treatment of these patients.

In this presentation my discussion will be limited primarily to two problems which certainly are not satisfactorily resolved at the present time. These are (1) the significance of brain damage in limiting the final goals of rehabilitation of the hemiplegic patient, and (2) the necessity for early attention to the muscular problems of the hemiplegic, together with some suggestions for obtaining adequate early treatment in the acute disease hospital without rehabilitation facilities. This discussion i based on my observations on 122 patients admitte to Elizabeth Kenny Institute from Jan. 1, 1956, t April 1, 1958. Since Kenny Institute is an inpatien rehabilitation facility not connected with an acut disease hospital, these were made mainly on thos patients who could not be treated satisfactorily i an acute disease hospital or an outpatient rehabili tation program. Of these, 105 were classified a having had cerebrovascular accidents includin thromboses, hemorrhages, and embolisms. Th conditions of the remaining 17 were ascribed t miscellaneous causes such as trauma, tumor, en cephalitis, brain abscess, congenital anomaly, o operation. There were 60 males and 62 females The paralysis was right-sided in 57 patients, left-sided in 64 patients, and bilateral in one. Their ages ranged from 3 to 80.

Brain Damage

The location and extent of brain damage determines the symptoms and physical findings in the patient. At first there is a period of flaccidity, which usually lasts for from 7 to 10 days. During this period, treatment directed toward prevention of contractures can be instituted with the best hope for permanent results. Therefore, the rehabilitation of the patient actually should be started during his stay in the acute disease hospital. During the sec-

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Director of Rehabilitation, Elizabeth Kenny Institute.

Chairman's address, read before the Section on Physical Medicine at the 107th Annual Meeting of the American Medical Association, San Francisco, June 25, 1958.

ond week spasticity usually develops. This will vary according to the severity of the lesion and the location of involvement and may be the major cause of disability. It is not possible to prevent spasticity if sufficient damage has occurred, but it is usually possible to avoid the development of contractures. Incipient tightness should receive vigorous treatment, beginning during the state of flaccidity, in order to prevent contractures which may totally incapacitate the patient.

Sensory areas in the brain may be involved with or without the involvement of motor areas. Loss of sensation and, particularly, loss of proprioception may cause almost as much motor disability as the destruction of motor areas. Occasionally a patient will manifest unilateral pain on the hemiplegic side. This is probably central in origin and is thought to be the result of thalamic involvement.

Right-sided hemiplegia is the result of damage to the left side of the brain. In a right-handed person this is likely to result in speech difficulty of the aphasic type as well as paralysis of the extremities. The casual observer usually gets the impression that the patient is mentally damaged because his speech is poor, he may not be able to recall the words necessary to express his thought, and his retention may be short. However, mentation is generally good in spite of severe speech difficulty. While difficulties in reading, writing, and arithmetic may be present, there is no difference between oral and written impairment. A great deal of work has been done in speech therapy for these patients. Many tests have been devised, from some of which, particularly that devised by Hildred Schuell,[1] a prognosis for recovery can be made with fair accuracy. Schuell's prognostic groups in aphasia are as follows: (1) defective recognition of names of common objects, no functional speech, reading, or writing; (2) impaired auditory retention span and auditory recall, resulting in defective speech, reading, and writing; (3) same as 2, with coexisting difficulty in recognizing and recalling symbols; (4) same as 2, with coexisting incoordination of speech movements; and (5) scattered auditory, visual, and motor findings, usually cranial nerve involvement, emotional lability, poor motivation, and limited initiative.

Aphasia is a complicated condition involving speech, hearing, writing, retention, abstract thinking, and recall of symbols and is undoubtedly not localized to any small area, such as "Broca's speech area." It should be remembered that handedness is not the only criterion for the so-called dominant hemisphere. A naturally left-handed person may be trained to be right-handed, and some individuals use the right hand for certain functions and the left for others. The location of the dominant hemisphere may be difficult to ascertain. In our series every patient with right-sided hemiplegia has exhibited some degree of language difficulty on Schuell's test battery. Sometimes the difficulties are not readily recognized on casual examination but require detailed testing because they involve functional loss in only a few of the higher level areas of speech formulation or auditory retention of longer materials.

Left-sided hemiplegia is the result of damage to the right side of the brain. Patients have no obvious speech difficulty if this is the nondominant hemisphere; therefore, to the casual observer, they seem to have a high degree of intelligence. There is no apparent mental damage because they are able to express themselves well, but careful examination shows some very serious defects, concerned with visuomotor, temporal, and spatial concepts and particularly with judgment and abstract generalizations related to these concepts,[2] which may cause more difficulty in rehabilitation than would loss of speech.

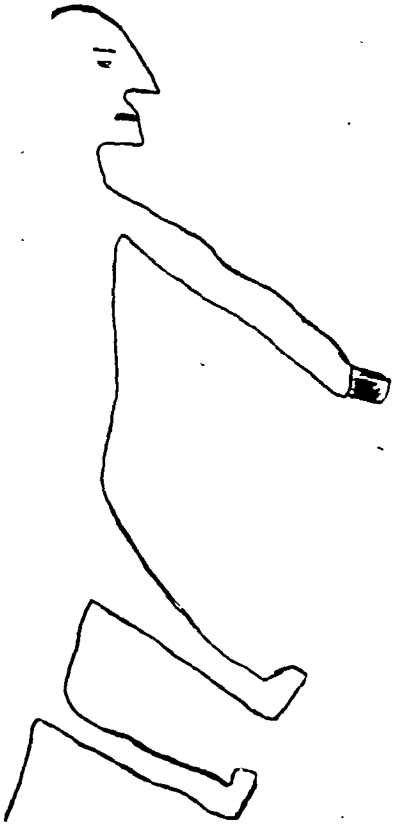
Fig. 1.—Drawing of man made by left-sided hemiplegic patient.

Visuomotor and spatial disturbances are manifested clinically by a tendency to ignore the left side of the body and objects on the patient's left. When drawing a man the left side is omitted or distorted (fig. 1). The patient may even state that the left arm and leg are absent although sensation is unimpaired. He may claim that the salad was omitted from the tray or that the fork is missing. Frequently the salad is not eaten although the patient admits he saw it; he states he just did not think of eating it.

He tends to bump into objects that are on his left and may pay no attention to a person standing to his left. When the person moves to the right side, he is included in the patient's sensorium. This is not the result of a left homonymous hemianopsia, although this defect may occur in some patients. When a patient is able to see perfectly well but has fundamental disturbances in visuospatial discrimination, not only does he ignore the person who is standing to his left or objects on his left but when reading a book he tends to omit the left side of the page, starting in the middle of a sentence, and, even more serious than this, he may not recognize his mistake. We had one patient who was an excellent artist before his hemiplegia who, when given a picture to paint in occupational therapy, started with the middle of the canvas and painted only to the right of the middle. Such persons should be evaluated thoroughly before being permitted to drive a car.

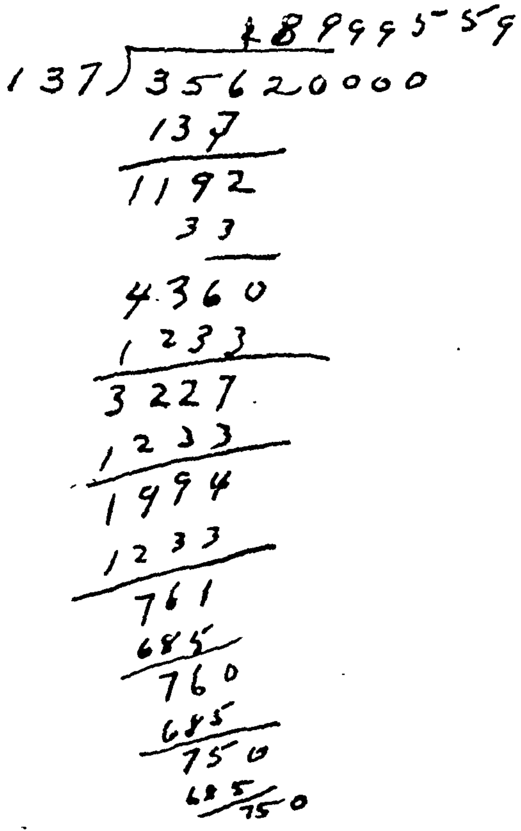

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Fig. 2.—Mathematical errors by left-sided hemiplegic patient.

These patients have serious difficulties with written mathematics. This again is concerned with spatial concepts, because the errors are often due to difficulty in arranging columns of figures in the proper order (fig. 2). Even more commonly they tend to become confused in the middle of the problem and change the arithmetic process; the first digit may be multiplied and the second digit added. They do not have the same disturbance in oral arithmetic. The same person who will make serious mistakes when writing down a problem may be able to solve it without error if it is "done in his head." These mathematical limitations are of great importance in certain vocations and certainly must be taken into account when the patient is returned to an occupation. For instance, the patient with left-sided hemiplegia should be studied very carefully before he returns to an occupation such as pharmacy, medicine, or accounting where mistakes in written mathematics may be serious. Again, the most serious drawback is the fact that the patient usually does not realize he has made a mistake and often cannot recognize it even when it is pointed out to him by the examiner.

Disorientation as to time concepts may not be obvious and therefore may be the cause of friction among various members of the staff and frequently between the patient's family and the staff. The patient may complain that he did not receive treatment at the specified time or did not receive certain types of care at all during the day. Accurate records are necessary to establish the actual facts. It is not uncommon for the family to refuse to believe that the patient is reporting inaccurately.

We find the patient's functional recovery depends more on the amount of brain damage than on the amount of extremity involvement, and these are not necessarily correlated. A patient with mild weakness and little spasticity may have impairment of memory to such an extent that re-training is almost impossible. For example, a woman was receiving occupational therapy twice a day, yet each time she came to the occupational therapy department she would look around with an expression of surprise and say "Well now, this is a nice place, why haven't I been here before?" It is difficult to get the left-sided hemiplegic patient back to employment in spite of his apparent intelligence and his verbal ability.

Employment

Twenty-three of these patients were judged to be physically able to return to work and were referred to the vocational counselor for evaluation and placement. Eleven had left-sided hemiplegia, one other was a left-handed left-sided hemiplegic patient, and 11 had right-sided hemiplegia. Of the 12 with left-sided hemiplegia, only 2 could be considered employed at the present time. One is attending the University of Minnesota and received satisfactory grades for her first quarter's work. The other is the left-handed, left-sided hemiplegic patient who was returned to work as a physician but receives close supervision of his mathematics and prescriptions by other members of his clinical staff. Since he is left-handed he probably should be classified with the dominant hemisphere cases, although his tests showed mild language and severe visuospatial defects.

Of the 11 patients with right-sided hemiplegia, 6 are now employed. Their occupations are hospital orderly, grain tester, bench worker, physician, executive, and baker's apprentice. Thus 2 of 12 patients with left-sided hemiplegia considered suitable for employment, or 16.6%, are actually employed (and one of these is left-handed and probably should be considered as having dominant hemisphere involvement), while 6 of 11 patients with right-sided hemiplegia considered suitable, or 54.5%, are actually employed at present. This series is admittedly small, and the statistics are not conclusive. However, it demonstrates the care that should be taken to analyze the cause of the disability when considering the probability of future employment. It also indicates that patients with dominant hemisphere involvement may be easier to rehabilitate vocationally than those with nondominant hemisphere involvement.

Physical Treatment in the Acute Stage

Typical upper extremity deformities consist of adduction and internal rotation of the shoulder and flexion of the elbow, wrist, and fingers. In the lower extremities the typical deformities are flexion of the hip, extension, or sometimes flexion of the knee and inversion and plantar flexion of the foot and ankle (fig. 3).

The first phase of treatment is directed toward the prevention of these typical deformities. This treatment should be started as early as possible, certainly before spasticity develops. This means within the first week after the onset of damage. It therefore must be done in the acute disease hospital, where there are usually no special rehabilitation facilities available. For this reason it must be carried on by the nursing personnel. This can be satisfactorily done if the nursing personnel has had some special instruction.

Use of Proper Bed.—On admission the patient should be placed on a bed that will not promote the development of deformities, such as a firm, long-fiber felt or foam rubber mattress resting on a sheet of plywood placed over the springs. Gatch beds should never be used and only a very small pillow should be allowed under the head. The hips must be straight and no pillows placed under the knees. If ambulation is to be successful we must be sure to prevent flexion contractures of the hip and knee. These are promoted by the ordinary hospital beds, particularly those where an inner-spring mattress allows flexion at the hip, or a Gatch position allows flexion at the hips and knees.

A special footboard should be used with a 6-in. wooden block to keep the mattress away from the footboard. This allows the foot to be kept at right angles without pressure on the heel while the patient is supine and also allows the foot to be placed against the footboard without resting on the toes when the patient is prone. One of the best methods for preventing hip flexion contracture is to have the patient lie on his abdomen for a period of time each day. There is usually a tendency for the lower extremity to rotate externally. This can be prevented by the use of a roll of toweling under the greater trochanter of the femur to keep the foot in a directly vertical position.

The upper extremity should be abducted, preferably at a right angle, with the forearm in external rotation, at least to a 45-degree angle. This can be accomplished by placing a pillow under the forearm and in the axilla. It is important that the wrist be in a cockup position and the fingers partially extended. This is done by fastening a hand roll around the patient's hand and wrist. The position should be maintained for as much of the day as possible when the patient is in bed.

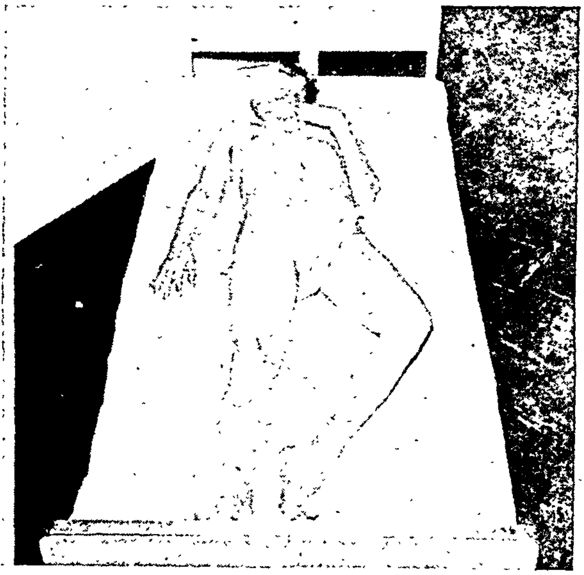

Fig. 3.—Typical deformities in hemiplegia.

Use of Hot Packs and Range of Motion Technique.—Application of hot packs should be started before the development of spasticity in order to prevent the development of contractures. At the same time, a full range of motion may be carried out passively. The nurse can be instructed in the range of motion so that this therapy can be maintained without any additional personnel. We have devised a technique whereby the range of motion exercises can be combined with the bed bath so that it does not take any material amount of extra time on the nurse's part. This is done very simply by moving the part through a full range of motion in each direction (flexion, extension, rotation, abduction, and adduction) first during the soaping of the part, again when the soap is washed off, and a third time when the part is being dried with a towel. If physical therapy is available in the hospital or if the patient can be transferred to a rehabilitation center, muscle reeducation can be given to those areas where function is not present. When voluntary function has developed, strength is increased by the use of strengthening exercises, particularly progressive resistance exercises.

Transfer from Bed to Wheel Chair.—A detailed technique for transferring from bed to wheel chair has been developed which we have found of great value, particularly in those patients who have a short attention span and require specific instruction for each portion of the movement. These patients cannot get out of bed just by being told to get out of bed. Each individual motion must be outlined in detail in order to make the transfer from bed to wheel chair successful. These steps are as follows: 1. The patient picks up the bad arm with the good arm. 2. He picks up the bad leg with the good leg. 3. He turns on his side. 4. He kicks his legs off the bed, using the good leg to assist. 5. He slides forward on the bed so that his feet will reach the floor. 6. He locks the brakes on the wheel chair. 7. He grasps the far arm of the wheel chair with the good hand. 8. He bends forward at the waist, keeping his head down, and reaches the erect position. 9. He pivots and sits in the wheel chair. 10. He unlocks the brakes and moves the wheel chair away from the bed. 11. He swings the footrest into place. 12. He lifts his foot onto the footrest. We use a footrest only on the involved side. The footrest is removed from the normal side. In this way he can propel the wheel chair using his good hand on the wheel and his good foot on the floor. These 12 essential steps are reversed in getting from the wheel chair into bed.

Ambulation Training.—Ambulation training is best carried on in a rehabilitation center or physical therapy department. If these are not available, however, nursing staff may start ambulation. When the patient is capable of carrying out walking exercises, he stands using parallel or hemiplegic bars or some other good support. He then performs the preparatory exercise of bending each knee alternately and returning to the straight position. He practices balancing on the bad leg and strives to bear weight on the bad leg just as long as on the good leg. It is important that the foot be flat on the floor. There is a tendency for the foot to invert because of overaction of the anterior tibial muscle, and if this occurs and there is some danger that the foot might come down on its lateral border, causing the patient to fall, a brace must be used. I usually start with a spring-type brace which is fastened to the shoe with a screw. In most cases this brace can be removed at a later date when the patient has gained better control. If permanent foot support is needed, I use a brace with an inside iron and outside T-strap. A long leg brace is usually contraindicated, for if the patient cannot walk without the brace he probably cannot walk with it. One exception to this rule is the patient who has pain in the knee from arthritis or some other cause which can be overcome by the use of an ischial weight-bearing long leg brace.

It is important when training the patient to insist on a gait which approaches the normal as nearly as possible. The patient should flex the hip and knee, bring the leg forward, dorsiflex the ankle, step down on the heel with the knee straight, rock forward onto the toe, and transfer his weight from leg to leg with an even rhythm. The common tendency of these patients to walk stiff-kneed with a circumducted gait should be avoided.

When the patient has mastered ambulation in the parallel bars or the hemiplegic bar, he progresses to the use of a crutch, if necessary, then a four-legged cane, then to the Kenny or Lofstrand cane and finally to a regular cane. If his ambulation becomes quite good he will walk without any support. The great majority of patients can be taught to ambulate in some fashion or other. Only a few are totally unable to ambulate, usually as a result of severe brain damage which limits memory and comprehension rather than because of severe loss of muscle control. We can devise gadgets to substitute for the physical but not for the mental disability.

Numerous devices have been invented for assisting the hemiplegic patient in self-care when the involved arm does not return to power. These include dressing devices, changes in the location of zippers and buttons so that the patient can reach them with the uninvolved hand, long-handled shoe horns, elastic shoe laces, hooks instead of eyelets for shoe laces, devices for fastening kettles and pans onto a table by suction so the patient can use them for mixing foods with one hand, and devices for brushing teeth and dentures, for combing hair, and for carrying on most of the other activities of daily living.

By the use of early and persistent treatment for the physical disability, and by employing ingenuity and imagination in the choice of assistive devices, the great majority of hemiplegic patients can be made self-sufficient, thus relieving their family and friends from the burden of their care.

Summary

Recent emphasis on rehabilitation techniques in hemiplegia has greatly improved the outlook for self-care and independence of these patients. Brain damage is the factor limiting recovery. Right-sided hemiplegic patients manifest speech and language defects but are more frequently returned to work than are left-sided hemiplegic patients, who exhibit visuospatial defects which militate against return

to competitive employment. A practical method of starting treatment in the acute disease hospital without specialized rehabilitation personnel is outlined, and a method of accomplishing partial self-care in the presence of severe retention loss is presented.

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EFFECT OF DIGITALIS AND DIURETICS ON EXERTIONAL DYSPNEA

STUDY IN AMBULANT PATIENTS WITH CHRONIC HEART DISEASE

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and
Leon Warshaw, M.D., New York

The value of digitalization and diuretics for the control of exertional dyspnea in patients with established chronic heart disease was studied in a group of 93 ambulant patients without auricular fibrillation. They were selected from a total of 204 patients with the diagnosis of congestive heart failure, in terms of the conventional criteria, on the basis that exertional dyspnea was the presenting problem, that physical signs of congestion were equivocal or absent, and that they were free of manifest complicating factors that might cause dyspnea. About three-fourths of them were in the older age groups with arteriosclerotic and/or hypertensive heart disease. In this type of patient long-term treatment with digitoxin failed to enhance the capacity for exertion without shortness of breath while the diuretic (meralluride sodium) afforded relief in many. A therapeutic test was suggested to detect those in whom prolonged treatment with diuretics should be pursued, also a similar test to detect the large numbers of patients who are commonly subjected to long and intensive treatment with digitalis materials, with high potentiality for toxic actions, but in whom there is little prospect of beneficial results.

This is a report of a study to ascertain whether digitalis or diuretics can increase the capacity for exertion without symptoms, in patients with chronic heart disease in whom physical signs of congestion are minimal, equivocal, or absent and whose presenting problem is exertional dyspnea.

The terms "heart failure" or "congestive heart failure" used in the text, unless otherwise indicated, refer to a clinical label applied to patients with heart disease, without regard to the behavior of the heart muscle that is implicit in these terms, for the terms stand for a clinical entity defined by signs and/or symptoms—accepted diagnostic criteria which are not always sufficiently discriminating to reflect the performance of the heart itself.

In congestive heart failure, breathlessness on effort is well known to be usually the earliest symptom. As the process advances it becomes increasingly troublesome and physical signs of congestion appear, such as pulmonary rales, enlargement of the liver, edema of the legs, and effusions into serous cavities. When such patients respond to digitalis therapy, the signs of congestion recede in whole or in part and the capacity for physical exertion without respiratory discomfort greatly improves. However, physical capacity is rarely, if ever, restored to normal. An element of diminished reserve in the form of exertional dyspnea usually remains, placing varying degrees of limitation on the patient's freedom to carry on in comfort. These patients, therefore, reveal two varieties of exertional dyspnea, one of which remains in the face of continued digitalization. The literature on heart disease and digitalis therapy draws no distinction between them in relation to either the mechanism or the utility of digitalization.

In accordance with conventional diagnostic criteria and concepts, patients with chronic heart disease who have become aware of breathlessness in the course of their habitual activities, provided complicating causes of dyspnea are excluded, are labeled as having congestive heart failure, even

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though they are now and may always have been free of physical signs of congestion. Their dyspnea is believed to result from impaired contractile force of the heart muscle (left ventricle). It is the common practice to place such patients on long-term digitalis therapy. We have pursued this practice in our cardiac clinics for many years. Under the usual conditions of management it is often difficult to escape the impression that digitalis has improved matters in a particular case, but there remains the fact that it is quite impossible to sort out the part digitalis plays in a therapeutic setting which involves several measures—chemical, physical, and psychological—applied simultaneously. Experience over many years with large numbers of ambulant patients with chronic heart disease classified as mild or early congestive failure, with equivocal or no signs of congestion but with persistent complaints and disability while under intensive treatment with digitalis, brought into focus the question as to whether digitalis was doing much to enhance their capacity to carry on without restriction due to shortness of breath. In many of these patients we turned to long periods of treatment with "placebo" tablets in the place of digitalis. The results left the effect of digitalis for the control of exertional dyspnea in patients of this category unimpressive and equivocal.

In the present study we examined the records of the past experience more closely. Also, in view of the striking results with diuretics in some varieties of congestive failure in which digitalis is ineffectual, we explored the effect of the diuretic alone on the exertional dyspnea of this type of patient and compared it with the effect of combined diuretic and digitalization therapy.

Study Group

The investigation was started in 204 ambulant adult patients with chronic heart disease in attendance at our two cardiac clinics; it covered a period of approximately three years. Of these patients, 82 turned out to be unsuitable for various reasons: insufficient data; irregularity in attendance; lack of reliability; complicating factors, such as infections, operations, hospitalization, severe angina of effort, acute coronary thrombosis, cerebral vascular accidents, anemia, pronounced psychoneurosis, primary pulmonary disease (nine patients), and congestive failure at rest (five patients); and marked physical signs of congestive failure, such as persistent pulmonary rales, edema of the lower extremities, marked enlargement of the liver, and paroxysms of nocturnal dyspnea. In addition, there were 29 patients with auricular fibrillation. Since these present the special problem of rate control, they were also excluded from the present analysis.

There remained 93 patients without auricular fibrillation, 91 with normal sinus rhythm, and 2 with complete heart block in whom we endeavored to ascertain the effect of treatment. In these, the physical signs of congestion were equivocal or inconstant, such as an occasional pulmonary rale, occasional and barely perceptible edema which may in some cases have been due to varicose veins, or inconstant finding of a palpable liver 1 or 2 fingerbreadths below the costal margin. These patients were free of symptoms at rest. Their presenting problem was shortness of breath on exertion. Weakness and fatigue were complaints in nearly all of them, but, in view of the fact that emotional factors play such a prominent role in these symptoms, the main emphasis was placed on the effect of treatment on their capacity for walking without respiratory discomfort as judged from the number of blocks or flights of stairs.

The diagnosis of organic heart disease was based on history (coronary thrombosis, rheumatic fever, syphilis, or other disease), physical findings (such as murmurs, embryocardia, gallop, or poor heart sounds), abnormal electrocardiogram (with such findings as bundle branch block, atrioventricular block, displaced S-T segments, or inverted T-waves), and fluoroscopic findings (including enlarged heart, tortuous aorta, aneurysm of the aorta, or distended hilar vessels), in accordance with conventional criteria.[1]

The common etiological classes of chronic heart disease were represented: rheumatic (5%), arteriosclerotic (27%), hypertensive (52%), and syphilitic (16%). Arteriosclerosis and hypertension with or without arteriosclerosis accounted for more than three-fourths of the group. The men and women were in approximately equal numbers (47 men and 46 women). The older age group was predominant, with the average age 63.6 years (range, 32-84).

Symptoms only were present in 42% of the group. In the remaining 58%, these symptoms were associated with minimal or equivocal physical signs of congestion.

Methods

The patients were allowed to carry on in their habitual manner without dietary limitation, except for recommendations leading to moderate restriction in salt intake. Their visits to the cardiac clinic were made at intervals varying from one to several weeks. The interval histories and examinations were in the hands of 12 physician members of the cardiac staff, who recorded their findings on a simplified clinic chart especially designed to elicit the pertinent interval information. This included the patient's statement as to whether the condition was unchanged, better, or worse; effort dyspnea, usually expressed in terms of number of blocks or flights of stairs giving rise to respiratory distress; weakness and fatigue; cough; orthopnea; nocturnal dyspnea; anginal pain; blood pressure; heart rate and rhythm; pulmonary rales; edema; and position of the liver edge. At each session the patient was weighed on the same scale by a clerk familiar with the importance of similarity in clothes and accuracy. Three senior members of the team supervised the prescribing in order to insure that the general plan of treatment was carried out. They recorded the medication prescribed and that which was actually received.

The plan of digitalization in the majority of cases was to give digitoxin, 1.2 mg. at one time, followed by a dose of 0.2 mg. daily, the dose increased or reduced as indicated by the response. In a few cases, tablets of digitalis leaf or digitoxin were employed.

The diuretic was meralluride (Mercuhydrin) sodium, given by intramuscular injection in most patients; in a few, mercaptomerin (Thiomerin) sodium was used. From previous experience with individual patient's reactions to these compounds, the doses during the investigation were sometimes 1 cc. and usually 2 cc. Some of the injections were given during the clinical sessions, others at the patient's home by the visiting nurse. The plan was to begin with an injection once a week and gradually shorten the interval in the endeavor to establish the lowest level of body weight corresponding to optimum symptoms. This sometimes resulted in an injection daily but, in most cases, two to three injections a week. When the more intensive schedules produced weakness or muscular cramps, the dosage was reduced or the intervals prolonged. Blood urea nitrogen levels were determined periodically throughout the course of therapy.

Although beneficial effects of a digitalis or diuretic regimen in terms of symptoms, physical signs, and weight loss should be in evidence in the first week of treatment, the ambulant patient is subject to so many factors which influence the course, such as fluctuations in physical and emotional stress and variations in diet and salt intake, that a reliable evaluation is not feasible from such short periods. After the first week the patient would often report that improvement had taken place and, in the next visit, that the condition seemed to be much as it was before the treatment. In the majority of cases, the periods of treatment were extended to months. Excessively long periods of treatment also posed problems in the interpretation of the results, due to what may be spontaneous improvement or progression of the organic disease and intercurrent complications. We found that in the majority of cases a period of four to five months usually provided a fairly level state on which the fluctuations from visit to visit were superimposed.

A curve fitted to the points representing the data obtained during these periods revealed whether the level with respect to symptoms and weight was the same as or different from the pretreatment level. The most decisive information was obtained when the curve leveled off after the first week or two of treatment, since in most patients the digitalization was carried out by a fairly rapid method. In the case of the diuretic, the matter of ascertaining the level, especially with respect to the change in body weight, was somewhat more difficult, since the optimum dosage schedule had to be determined in each patient and that often took several weeks. Once the schedule reached two or three injections during the previous week, the lower level of body weight caused by the drug was usually unmistakable, and this helped to rule out those few in whom coincidental anorexia or progressive malnutrition might be a source of error in judging the effect of the drug.

A word is in order about the data on the symptom of exertional dyspnea and minimal physical signs. The circumstances under which this study took place did not provide for the "double-blind" test usually essential for the satisfactory control of bias and the psychological effects of treatment.[2] There were several reasons. The need for a more systematic examination of the problem crystallized only gradually out of impressions that seemed out of line with common belief and practice which we shared for many years.

In evaluating the effect of digitalis alone and the utility of a "placebo" tablet in the same patients, we found it expedient to call on records made in many cases prior to the beginning of this investigation, simply applying to the closer examination of the facts the more revealing method of the curve fitted to data recorded at frequent intervals over periods of many months. In connection with the diuretic treatment, we had planned to depend on the loss of body weight, an objective measurement, as a means of support to the evidence of clinical improvement, since in the study of the more pronounced grades of congestive failure[3] the gradual fall of body weight runs fairly parallel with clinical improvement, but this proved unsatisfactory in the patients of the present study—those with few or no physical signs of congestion. In them, the loss of body fluid was often unattended by any manifest evidence of subjective improvement. There was also the ethical issue[4] of an intramuscular injection of a somewhat irritating "placebo" several times a week for periods of months with the discomforts and risks inherent in any injection.

The nature of the problem and the manner in which it was pursued, we believe, reduced to a minimum the influence of bias and suggestion. The drugs were not new ones and were free of the psychic charge of current and exaggerated claims of new proprietaries. The clinic's physicians had used them repeatedly in the casual manner of commonly accepted therapeutic agents in the same patients before they were assigned to the study series. The blunted enthusiasm of the physician for conventional remedies has its blunting effect in the patient on the power of suggestion. The study chiefly involved the insurance of optimum dosage, systematization of dosage and courses, and methods for eliciting and recording data to improve their accuracy and to facilitate analysis. Consistent bias in relation to the interpretation of the patient's account of symptoms was under some control by the fact that it was often a different physician who looked after the patient at the various clinic visits. In relation to the mercurial diuretic, the psychic effect of an injection was always present as a possible source of improvement in symptoms by suggestion.

Again, the plan involved only an increase in the number of doses of an injection which the patient had received many times before the study. Further, the patient's opinion often helped to decide the course to be followed, namely, that the injections should be continued even though they were troublesome and sometimes painful, that four or five injections a week provided no greater relief than two but that two a week were more effective than one, or that the injections should be discontinued because of their failure to provide any appreciable relief. Such quantitative features are not in the usual nature of the therapeutic response to suggestion. Nevertheless, the absence of strict adherence to the "double-blind" test remains a defect with respect to the definitive nature of the conclusions, and we present the results as an account of experience which may serve the purpose of arousing interest in the further reevaluation of the utility of digitalis and diuretics in the type of cardiac patient we have described, as well as in several other forms of heart disease in which their use is commonly taken for granted but in which their usefulness calls for more satisfactory proof.

Table 1.—*Effects of Digitalis and Diuretic Therapy in Ambulant Patients with Heart Disease*

	Digitalis (44 Patients)	Diuretic (92 Patients)
Physical signs of congestion		
None, %	52	41
Minimal, %	48	59
Sex		
Males, %	54	50
Females, %	46	50
Age		
Av., yr.	63.6	63.6
Range, yr.	38-84	32-84
Etiological type of disease		
Arteriosclerotic, %	39	27
Hypertensive,* %	43	51
Rheumatic, %	2	6
Syphilitic,† %	16	16
Period of treatment		
Av., wk.	15	19
Range, wk.	1-52	3-44
Change in condition		
Improvement in exertional dyspnea, %	...	54 (of total)
Improvement in signs of congestion, %	...	22 (of 54)
Loss of body weight, %	...	90 (of total)
Av., lb.	...	5.5
Range, lb.	...	1-13

* Includes those with and without arteriosclerosis.

† Includes those with syphilitic heart disease with aortic insufficiency or aneurysm and those with hypertension and/or arteriosclerosis with only positive serologic findings as evidence of syphilis.

Results

As already indicated, the changes in symptoms and body weight often showed wide fluctuations from visit to visit, the patient's judgment of the interval condition being sometimes the "same," sometimes "better," and sometimes "worse" and similarly for the number of flights of stairs or blocks before dyspnea appeared. In the average period of approximately four to five months with each course of treatment, the patients made an average of 16 visits, in some more than 40 visits. The data thus obtained provided the points to which a curve was fitted as a means of evaluating the effect of the particular course. The results are summarized in the tables. They refer only to ambulant patients with established heart disease without auricular fibrillation but with exertional dyspnea, in whom physical signs of congestion were minimal, equivocal, or absent, and most of whom had never been in a state of congestive failure with the classic signs of congestion requiring a course of bed treatment.

In most of the 44 patients who were under continued digitalis therapy for a period of nearly four months, there were similar periods of medication with a placebo tablet. The data from all but eight patients were obtained in the course of their routine management prior to the beginning of the present study. It was the unimpressive difference between the effects of the digitalis and the placebo that aroused our suspicion of the value of digitalization in this variety of exertional dyspnea. Closer examination of these data and the evaluation of the results from curves fitted to the points obtained at the various clinic visits confirmed the earlier impression. As may be seen in table 1, there was no material change in body weight, physical signs of congestion, or capacity for exertion without breathlessness that could be ascribed to the long course of digitalis medication.

The effect of the diuretic alone is also analyzed in table 1 in a group of 92 patients, including the 44 in whom digitalization was studied. The intramuscular injection of meralluride without digitalization was given over an average period of nearly five months. Indecisive response was included among data for those who showed no appreciable improvement. Unmistakable improvement in exertional dyspnea occurred in approximately one-half of the patients. Among those that showed some physical signs of congestion, in approximately one of five there was some clearing of the signs. The body weight decreased in most of them to a level averaging approximately 5 lb. (2.3 kg.) below that of the prediuretic period. This effect was not always accompanied by relief of exertional dyspnea.

In 73 of these patients, a course of treatment with the diuretic alone was followed by one in which digitalization was added to the regimen. These results are summarized in table 2. The two courses covered an average period of nine months, five with the diuretic alone and four with the combined therapy. With the diuretic alone, the results were similar to those mentioned above. Most of the patients maintained a reduced level of body weight, averaging nearly 5 lb. About one-half of them experienced improvement in capacity for exertion without breathlessness and about one in five some recession in the physical signs of congestion. During the period in which digitalization was added, in about one-half of the patients the dosage of the diuretic was reduced with the view that this would provide a more favorable condition for detecting an effect of digitalization. A few patients showed some further decrease in body weight, while a larger number showed an increase averaging about 3 lb. (1.3 kg.). With respect to exertional dyspnea and the physical signs of congestion, the addition of digitalization to the diuretic treatment produced no further improvement.

Comment

Limitations of Digitalis.—The striking response to digitalis by most patients with heart failure showing the classic signs of congestion, such as pulmonary rales, enlarged liver, and edema of the legs, especially in those with auricular fibrillation and rapid ventricular rate, and the experimental demonstration that digitalis improves the contractile performance of heart muscle have provided the basis for wide expansion in the scope of its clinical applications. Belief in the universal usefulness of digitalis for the treatment of heart failure has become so firmly entrenched that its utility is taken for granted and little inclination remains for systematic evaluation of its effectiveness in the wide variety of types of heart diseases bearing the label of congestive heart failure. The drug has also been put to other uses in heart disease. It has been advocated in heart disease without evidence of failure as a prophylactic against failure or cardiac enlargement[5] and as a means in such cases to improve the mechanical efficiency of the heart.[6] It has also been suggested as a test for the detection of heart failure. For example, in patients with cor pulmonale in whom congestive failure may ensue to increase the marked dyspnea due to the primary pulmonary disease, the absence of symptomatic improvement after digitalization is presumed to exclude heart failure.

This would all be reasonable if it did not involve an oversimplification of the nature of clinical heart disease classified as congestive failure and of the physical-chemical state of heart muscle leading to failure of contractile force. There is considerable experience[7] which indicates that these represent not a single but a multitude of mechanisms, some of which are reversed by digitalis and others not. A few examples may be cited. On the experimental side, there are numerous observations of what appear to represent a variety of physical-chemical states in heart muscle in which digitalis does not affect contractile force.[8] The papillary muscle of the cat's right ventricle made to contract in a medium of blood serum shows little tendency to lose or to increase its force when digitalis is added, while, when it is in a medium of Ringer's solution, contractile force rapidly declines and is promptly restored by the addition of digitalis. In this preparation, higher concentrations of digitalis itself cause a rapid decline in force. Failure caused by high concentrations of potassium is not reversed by digitalis glycosides; this is also the case in failure caused by quinidine, until the state of incomplete recovery is achieved after the removal of the quinidine.[7c]

TABLE 2.—*Comparison of Effects of Diuretic Therapy Alone and Combined Diuretic and Digitalis Therapy in Seventy-three Patients**

	Diuretic Therapy	Combined Therapy†
Period of treatment		
Av., wk.	20	16
Range, wk.	3-43	1-40
Change in condition		
Improvement in exertional dyspnea, %	53	...
Improvement in signs of congestion,‡ %	22	...
Body weight		
No change, %	...	65
Loss, %	89	12
Av., lb.	5.4	1.8
Range, lb.	1-13	1-3
Gain, %	...	23
Av., lb.	...	3.2
Range, lb.	...	1-8

* Includes men, 48%, and women, 52%, with these etiological types of heart disease: arteriosclerotic (25%), hypertensive, with and without arteriosclerosis (53%), rheumatic (7%), and syphilitic, with aortic insufficiency or aneurysm and with hypertension and/or arteriosclerosis with only positive serologic findings as evidence of syphilis (15%).

† Diuretic dosage reduced in this period in 45% of patients.

‡ 46 patients (63%) originally showed minimal physical signs of congestion; 27 (37%) showed no signs.

On the clinical side, the evidence that digitalization improves matters in the case of mitral stenosis with dyspnea, pulmonary rales, or attacks of pulmonary edema is unimpressive; this is also true in the congestive failures associated with adherent pericardium, cyanotic congenital heart disease, acute coronary thrombosis, active rheumatic carditis, severe thyrotoxicosis, thiamine deficiency (the beriberi heart), and several varieties of chronic, far-advanced heart disease. Some of these may represent mechanical obstacles to improvement in contractile force; some, extracardiac factors, such as renal failure which maintains the state of congestive heart failure; and some, physical-chemical changes in heart muscle which are not reversible by the steroids of the digitalis group.

These suffice to point up the fact that the utility of digitalis in the various stages and types of heart disease labeled congestive failure cannot be taken for granted and that each calls for a direct investigation.

The absence of evidence of any notable increase in myocardial force by digitalis in far-advanced congestive failure ("intractable failure") has received considerable attention in recent years.[9] The present study deals with the cases clinically labeled as congestive failure but at the opposite extreme of the spectrum, the mild or early cases, those with extertional dyspnea only, with minimal, equivocal, or no physical signs of congestion. The results show that one variety of these is in a sense also "intractable" to digitalis action. Nothing is known of the mechanism to explain the failure of digitalization to affect exertional dyspnea in these cases. There is the possibility that they represent a phase of impaired contractile force of heart muscle of a physical-chemical nature uninfluenced by digitalis or that the contractile force of their heart muscle is normal and that, in chronic heart disease, adaptive changes take place not only in the rate, shape, and size of the heart but in the general circulation involving such factors as speed of adaptive response to exertion, redistribution of blood, or thoracopulmonary changes which may give rise to exertional dyspnea.

Diuretics in Exertional Dyspnea.—In another study of far-advanced congestive failure in which digitalis was without effect, we examined the effect of salt restriction with daily injections of the mercurial diuretic without digitalization.[9c] The symptoms, the edema, and the other reversible signs of congestive failure cleared rapidly. The total clinical result was indistinguishable from that in cases in which digitalis was included in the regimen. The digitalization of these patients before discharge from the hospital produced no further clinical effects. Others[10] have described similar experience with diuretics alone but have suggested that the results had only the appearance of a restored circulation and that, in a physiological sense, congestive failure remained.

In the present study, ambulant patients with chronic heart disease and exertional dyspnea with minimal or no physical signs of congestion were treated with the mercurial alone without digitalis for periods of several months. This increased the capacity for exertion without breathlessness in varying degrees in approximately one-half of the group. The addition of digitalization to the regimen in courses of similar duration produced no further clinical effects. The body weight during the diuretic regimen remained at an average level approximately 5 lb. below the prediuretic period. These results indicate that the mechanism accounting for the exertional dyspnea in many of these cases is an unfavorable amount of extracellular fluid. Whether the extracellular fluid volume in these cases is within the range of the normal or lies outside of it, as in frank edema, remains to be established. A noteworthy feature of the results was the observation that, while in some the symptoms and gain in weight appeared fairly promptly after the diuretic was discontinued, in others the lower weight and improved capacity for exertion persisted for several weeks after the course was interrupted, a fact which indicates that the reduction in extracellular fluid volume or the clearing of edema with diuretics not only is a symptomatic treatment, as has sometimes been suggested, but restores a better circulation and that an unfavorable amount of extracellular fluid in heart failure not only is an effect but may also, in turn, become a cause of congestive failure. In line with this is the fairly common experience of congestive failure precipitated by intravenous saline solution infusions and measures which promote salt retention.

The Practical Problem.—Since there appear to be two varieties of exertional dyspnea in heart disease, for only one of which digitalis is useful, there are the problems of deciding which one it is when a patient with heart disease without physical signs of congestion presents this symptom and of deciding when the responsive type has been superimposed on the nonresponsive one. No completely satisfactory means exists for ascertaining these facts. A history of an attack of failure with the classic physical signs of congestion and a period of bed treatment helps to decide the issue, for such patients without a maintenance regimen of digitalis tend to relapse into failure with congestion. Without such a history, a therapeutic trial is the most direct method for obtaining the information.

The ambulant patient may be digitalized with 1.0 mg. of digitoxin given at one time or, as some prefer, in divided doses, followed by a daily dose of 0.2 mg., with the maintenance dose increased or reduced as indicated by the response. Its use for two or three weeks should usually suffice to supply an answer to the question as to whether the capacity for exertion without breathlessness has been enhanced. If a decisive negative answer is obtained, the drug therapy should be discontinued. If the response to the digitoxin is equivocal, a placebo should be tried for a similar period. The proper choice of a "placebo" is an important factor.[11] If a positive answer is obtained with the digitoxin, it may be planned to continue the drug therapy indefinitely, although it is well to try the patient on a placebo for a similar period to rule out the effect of suggestion. It is desirable and often feasible to try the placebo first, because the lasting effects of a course of digitalization may confuse the answer concerning the effect of the placebo. These expedients will insure the detection of those patients in whom long-term digitalization is necessary and, at the same time; the vast group of patients with chronic heart disease in whom exertional dyspnea is uninfluenced by digitalis and who are often needlessly exposed for long periods of time to these potent drugs with high potentiality for toxic effects.

In patients in this latter group who fail to benefit from the digitalis, a diuretic may be tried with the expectation of varying degrees of relief of exertional dyspnea in many. Again, a trial for two or three weeks should suffice to establish whether it is sufficiently useful to continue in the particular patient. As in the case of digitoxin, a positive or equivocal result should be checked against a course of placebo medication for a similar period. In this study we employed the mercurial diuretic by injection to insure the most effective results. One or another of the oral diuretic agents, such as chlormerodrin (Neohydrin), amsometradine (Rolicton), ethoxzolamide (Cardrase), or chlorothiazide (Diuril), in full dosage may often serve the purpose. In case of doubtful results, a trial of the organic mercurial by intramuscular injection two or three times a week for two or three weeks should usually decide the desirability of continued treatment with the diuretic agents.

The emphasis on the action of digitalis materials to increase the contractile force of heart muscle and on the striking results from their use in the treatment of some forms of congestive heart failure, with scant attention paid to the few reports pointing to the limitations of these drugs, has established and sustained the view that the clinical diagnosis of heart failure is always an indication for digitalis medication. It has also had the effect of diminishing interest in pursuing critical observations to evaluate its efficacy in the various heart diseases bearing the label congestive heart failure.

The utility of digitalis in cardiac patients with the clinical diagnosis of heart failure in different stages, phases, and types of disease cannot be taken for granted. The clinical diagnosis of congestive failure represents a variety of mechanisms which may not always involve failure of contractile force, some of which are responsive to the drug while others are not. Moreover, failing contractile force of heart muscle has several mechanisms, some of which do not react to digitalis.

Summary

Large numbers of cardiac patients exposed for indefinite periods to intensive treatment with digitalis, with high potentiality for toxic effects, often show little evidence of therapeutic benefits.

The effect of digitalization was studied in a group of 93 patients with established heart disease without auricular fibrillation, bearing the diagnosis of mild or early congestive heart failure, in accordance with conventional criteria. They were selected on the basis that physical signs of congestion were minimal, equivocal, or absent and that one of their presenting problems was limitation in physical capacity by breathlessness on exertion. About three-fourths of them were in the older age groups with arteriosclerotic and/or hypertensive heart disease.

These patients were treated with various courses, each for periods of several months: digitalization alone; placebo tablets; a diuretic alone, meralluride (Mercuhydrin) sodium, by intramuscular injection; and combined therapy with the diuretic and digitalization.

There is a variety of exertional dyspnea, most clearly seen in patients with chronic heart disease with few or no physical signs of congestion, which is uninfluenced by digitalis but is frequently brought under varying degrees of control by diuretic therapy.

The clearing of edema by a diuretic is not only a symptomatic treatment. An unfavorable volume of extracellular fluid not only is an effect but may in turn become a cause of the condition that bears the clinical label congestive heart failure.

In patients with heart disease with few or no physical signs of congestion and with breathlessness on exertion as a presenting symptom a therapeutic test was used to detect those in whom continued digitalis medication would be effective and necessary and also the large group of those in whom digitalis would offer no prospect of beneficial effects. A similar test was used to detect the patients in the group nonresponsive to digitalis in whom some relief from exertional dyspnea would be possible by long-term treatment with diuretic agents.

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STUDIES IN HUMAN ISOLATION

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Procedures for studying isolation vary, and there is no typical laboratory isolation. The degree of contact between the isolated subject and his environment, especially his observers, must be defined in terms of distances, times, limitations of visual, auditory, and kinesthetic inputs, means available to the subject for structuring his isolated existence, and especially his ability or inability to terminate isolation when he wishes. Communication of any kind counteracts the effects of isolation, and when subjects know they are being observed they do not feel truly isolated. If communication or feedback to the subject is distorted, the situation becomes more stressful, and profound feelings of anger and anxiety can be produced. Experimentation in this field yields new data on individual differences, reveals the generally felt need of people for a structured environment, and is of importance in military medicine.

The isolation of man from his accustomed environment has profound impact on the functions of his mind. Many circumstances in real life entail such isolation. Their effects have many names, from "nostalgia" to "desert madness," and range from mild feelings of anxiety and depression to hallucinations, delusions, and even death by suicide.

The armed services have long been concerned with operational situations and accidents of war involving radical environmental change and have sponsored studies of sailors lost at sea, men confined in submarines, and prisoners of war.[1]

Special interest has been directed to the methods employed in Communist prison camps. The prisoner was trapped in a foreign land and foreign culture. He was subjected to a program seemingly designed to increase the degree of isolation. Letters from home, packages from the Red Cross, military discipline, and organization among the prisoners were severely limited. Thus, the prisoner was denied the usual means of maintaining his "self-concept." He was rewarded and punished with reference to an entirely strange set of standards. In this way, his "self-esteem" was attacked. Periods of solitary confinement, physical hardships, and illnesses further impaired mental functions.[2]

The effectiveness of these techniques in controlling or converting military and political prisoners has helped stimulate experimental studies of certain

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aspects of isolation. Heron and co-workers,[3] Lilly,[4] Vernon and Hoffman,[5] Solomon and associates,[6] and others have conducted experiments in "artificial isolation." In these studies men were separated from their usual immediate surroundings by reduction in the level or variability of sensory input. These situations have been described as "sensory deprivation."

There has been no standard procedure for studying isolation, and there is no "typical laboratory isolation." Visual, auditory, and kinesthetic inputs have been limited by various techniques. The degree of contact between subject and investigator has varied, as has the duration of the several groups of experiments. The subjects, who sometimes were the investigators themselves, had varied backgrounds. In experimental situations the subject has always been able to terminate isolation when desired.

Although experiments lack the essence of reality, the subject is still removed from his usual environment and loses many frames of reference and means of structuring his existence. In some of these experimental isolation situations, fairly rapid onset of distorted perceptual and intellectual functions occurred.[7] In others, little effect on the subject was noted.[5]

Extension of flight range has increased the significance of isolation in aviation medicine. Crews on prolonged missions are exposed to a restricted, monotonous sensory field. It has been suggested that this type of isolation might be a contributory factor to "pilot disorientation," which not infrequently is cited in aircraft accident reports. Pilots flying at high altitudes may also report what has been called "the break-off phenomenon" or high altitude dissociation. Furthermore, space crews will be subjected to an artificial environment that will be isolating in many ways.

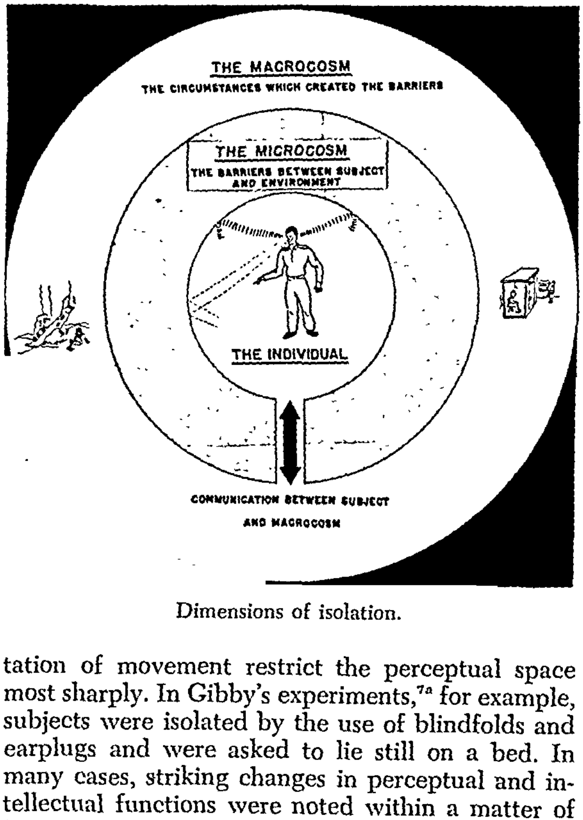
Because of the many military operations in which the complex problem of isolation is an important feature, it would appear desirable to review the variables and parameters pertinent to research in this area. It is helpful to group them into four major dimensions (see figure), which will be described more fully below. The first dimension consists of the barriers between the subject and the outside world—the means by which he is isolated. We have termed this the "microcosm." The second dimension refers to the individual who is isolated. The third includes the reality factors of the outside world—the conditions, circumstances, reasons, and attitudes under which isolation occurs. We have termed this dimension the "macrocosm." The fourth dimension refers to communication between subject and macrocosm.

The Microcosm

The microcosm is the environment apparent to the isolated subject. It includes the physical structure of the place of confinement; the limitations imposed on the subject's perceptual functions; the actual modality, quantity, and pattern of sensory input; the duration of the situation; and the tasks given to the subject.

Occasionally, subjects experience a claustrophobic reaction when confined in a small space. Also, a cramped facility may produce intolerable physical discomfort. During one series of experiments in the Aero Medical Laboratory, subjects sat in a chair for periods of four to six hours. Since this was quite uncomfortable to some subjects, these experiments were concerned with tolerance of discomfort as much as with sensory deprivation.

The space available in which the individual can perceive defines a different parameter, which we refer to as the "perceptual space." Infinite and monotonous surroundings, such as the sea, are isolating in one way, while a dark and quiet room is isolating in another. Blindfolds, earplugs, and limitation of movement restrict the perceptual space most sharply. In Gibby's experiments,[7a] for example, subjects were isolated by the use of blindfolds and earplugs and were asked to lie still on a bed. In many cases, striking changes in perceptual and intellectual functions were noted within a matter of hours. The subjects of Heron and co-workers,[3] on the other hand, wore frosted goggles and were close to a speaker which produced a masking noise. They were fed and tested at intervals outside the room in which they were isolated. These subjects experienced changes in perceptual function and difficulty in creative intellectual activities after a day or so.


THE MACROCOSM
THE CIRCUMSTANCES WHICH CREATED THE BARRIERS
THE MICROCOSM
THE BARRIERS BETWEEN SUBJECT AND ENVIRONMENT
THE INDIVIDUAL
COMMUNICATION BETWEEN SUBJECT AND MACROCOSM

Dimensions of isolation.

The Aero Medical Laboratory facilities include a dark and soundproof chamber. It contains a bed, chair, refrigerator, and chemical toilet. We have done 54 experiments in which subjects remained inside continuously for as long as seven days. Tests of intellectual functions carried out within one-half hour after isolation have revealed no striking changes. However, most subjects do report a loss of the sense of urgency to think; they "don't care and don't think" while isolated. Unusual perceptual phenomena have not been found.

It may be that the position of the barrier to sensory input is psychologically significant. That is, the blindfolded subject, with a minimal perceptual space, may feel naked and defenseless and be more prone to psychological changes, while a subject enclosed in a quiet, dark room may feel protected.

Loss of cues from one modality of sensation may give rise to overemphasis on cues from other modalities. When there is a reduction in the total number of cues available, the subject may be expected to strain for stimuli. However, the effects of restriction of the various modalities must be carefully analyzed for the unique psychological significance these individual sense organs have for each subject. The inability to see, for example, may be especially threatening to certain individuals.

Change in pattern of sensation can be produced either by reducing the intensity and variability of stimulation or by the addition of monotonous masking cues. The monotony of repetitive stimulation may give rise to one group of reactions, whereas continuous presentation of amorphous stimuli may give rise to others.

It should be emphasized that reduction in number or variability of sensory stimuli must not be interpreted merely as an alteration of "inputs" to a brain viewed as a computer. For stimulus reduction also disrupts psychologically significant relationships of the subject with his environment.

Our data indicate that time in isolation is important in several ways. First, the longer the isolation lasts the more stressful it becomes. Second, if the subject knows the planned duration of the experiment in advance, isolation is easier to tolerate. Also, an experiment scheduled to last as long as the subject will stay in provides an entirely different kind of experience. Third, we have seen that, during the first day of isolation, the subject's "built-in clocks," such as desire to urinate, eat, and sleep and the rate of beard growth, are sufficient to give him some idea of the time. After a day or so, however, the subject becomes "lost in time." This is an entirely different kind of stress from sensory deprivation per se. When this has occurred in the framework of the isolation experience, it has been the most stressful aspect of the experiment. Fourth, any experiment in which the subject had no control over duration—that is, an *experiment he could not terminate at will*—would be a still different and potentially more stressful situation.

The last feature of the microcosm refers to tasks given to the subject. These may completely change the nature of an isolation experience. For example, an early group of our subjects, who were asked to signal when they thought each half-hour had passed, spent much of their time determining when to press the button. This created an undesirable degree of structuring in the experiment.

The Individual

Reviews of isolation in real life by Lilly[4] and Solomon and co-workers[6] point out that the personality of the individual subjected to isolation is important in determining how he will respond to the situation. It is said, for instance, that those who have a strong self-concept, yet who can become passive, do the best. Experimental isolation offers a unique opportunity to observe individual variations in behavior.

In our experience, schizoid subjects have found the procedure extremely stressful. Two have terminated the experiment within two hours. These subjects seemed most highly dependent on familiar environmental settings.

Passive-dependent individuals have seldom found short periods of isolation stressful, although some have complained of boredom and physical discomforts and have expressed anxiety that the experimental situation might have been manipulated in some way they were not expecting. For them, the most significant aspect of the situation seemed to be their relationship with the experimenters and their desire to appear to have done well.

Compulsive subjects have expended great effort in structuring the situation around tangible bits of reality. Some folded paper, counted or devised other methods to mark the passage of time, spent excessive time manipulating their food, exercised, or tried to force themselves to think in a planned fashion.

Many of our subjects have been strongly motivated Air Force officers. They have regarded the experiment as "just another mission" in which they try to do as well as possible. As a group, these subjects have been rather comfortable in the experimental situation.

When our experiments have been allowed to last until the subjects terminate them, reasons given for termination have not been well founded in reality. Subsequently, subjects have recognized this and either have searched for another reason or have explained that "though the reason seems unimportant now, it wasn't then." Termination was usually an impulsive, emotionally loaded event. Some of the reasons given might be called symptoms; they included intolerable boredom, somatic complaints, extreme anger toward the experimenters, and profound anxiety.

When the subject first enters isolation he is usually somewhat anxious, just as anyone might be when placed in completely new surroundings. He is confronted with an indefinite, rather unstructured emptiness which he then "fills with himself." He uses characteristic modes of operation or devices of defense and exaggerates them to become, in a way, "more like himself." Reminiscences, day residues, and little problems are the most common thought contents.

As time passes, these means of maintaining usual mental functioning seem to become inadequate. Or, in theoretical terms, as Rapaport has written,[8] autonomy of the ego from the id is threatened when there is a lack of essential environmental stimuli. It appears that meaningful environmental structure is necessary for the ego to cope with id impulses. Release of id impulses would seem to be the reason that termination is inevitable and the subject's explanation of it often irrational. Shortly after the subject ends the experiment, restructuring, rerepression, and a return to usual modes of functioning occur.

The individual's pattern of response can usually be predicted from the psychiatric interviews and psychological tests which are part of each of our experiments. In a sense, then, isolation is analogous to a projective psychological testing technique.

The Macrocosm

The macrocosm consists of the reality factors, that is, the surrounding environmental circumstances in which the microcosm occurs. For example, any isolation experience may be expected or unexpected, planned or accidental, purposeful or capricious, good or bad, right or wrong. More specifically, the various real-life experiences have unique "sets" or "expectancies," such as being a prisoner (the world is unfriendly) or being lost (the world is unknown). Similarly, an experimental isolation procedure thought of by the subject to be a straightforward study of sensory deprivation is entirely different from a situation in which the surroundings appear mysterious and are anxiety-producing. An important variable in isolation, the degree of feeling "aloneness" which the subject experiences, depends largely on the combination of circumstances which make up the macrocosm.

Further, in experimental situations, the training or specialty of the experimenters, their relationships with their subjects (transference and countertransference), and the reasons they have undertaken the study contribute to the "set" and may influence the outcome of the procedure.

Also, varied interests of the experimenters have led to a wide range of conceptualizations concerning isolation. Heron and associates[3] speak of isolation in terms of inadequacy of sensory input for maintaining usual brain function. Lilly[4] writes of dependence on reality for maintenance of ego structure. Solomon and co-workers[6] and Gibby[7a] consider more fully individual variations in reaction to a given experimental situation.

Communication

Communication between the microcosm and the macrocosm is the last dimension to be discussed. Communication of any kind is anti-isolation in effect. We have compared isolation situations in which the subjects were aware that they were being monitored with those in which they were not.

When subjects knew they were being observed, in any way, they did not feel alone or truly isolated. Thus, even one-way communication from the inside out may alter the isolation situation. We have recorded skin resistance continuously. Several subjects have reported to us that, since they knew that the wires to the skin resistance meter conveyed information, they felt "connected with the outside." If communication or feedback to the subject is distorted, the situation becomes much more stressful and profound feelings of anger and anxiety can be produced.

Summary

The study of human isolation confronts workers in the field with an almost unlimited number of variables and parameters to be controlled or at least considered. These include the details of the isolation, all aspects of the personality of the subjects, and the concepts and feelings of the experimenters. It is a unique tool for the study of personality and of the needs people have for environmental structure. This type of research has potential applicability in military medicine.

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COMPUTERS IN MEDICINE AND BIOLOGY

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Problems hitherto insoluble because of the formidable amount of calculation involved can now be left to machine computers of either the analog or the digital type. Both types are being applied to medical problems. They not only speed up calculations but can also be wired in such a way as to simulate biological regulatory systems and to incorporate any desired hypothetical reaction-pattern to stimuli. The complex interaction of factors affecting blood pressure, respiration, and other functions can be represented in circuitry that stores information, processes it at high speed, and retrieves both the information and the results from storage promptly and accurately. The machine-computer and the human brain differ in the way they handle inexact data: the brain can usually still make a qualitative analysis and arrive at a conclusion, whereas the computer would report only nonsensical results. The examples here given show that every field of medical science and the healing arts is likely to gain if every original worker will be alerted to the possible application of these new tools in his own field of endeavor.

Although the first computer device, the abacus, was in use over 2,000 years ago, the first computers which were in any sense automatic date back only to the 17th century, when Pascal and Leibnitz developed multiplying machines. In 1834, Charles Babbage conceived of a machine which was strikingly similar to the modern digital computer. The punched card system of data processing was invented in 1889. Mechanical calculating machines originated at the same time. Although refinement in data-processing techniques had evolved, it was not until World War II, when military considerations stimulated technological progress, that the great advances in computer art were achieved. With the advent of the jet and missile age, the Air Force in particular has directed great effort toward the perfection of computer capabilities able to predict the relation between design and performance of aircraft without the actual construction of prototype models. An illustration of the rapid growth of the field may be seen in the fact that as recently as 1945 it was possible for practically all the computer specialists in the United States to know each other personally. At present, with about 250 large scale computers in operation in the United States, it has become difficult even to know all the new facilities which have become available.

Modern high speed electronic computers have been widely applied in industry and are finding increasing application in the physical sciences. They are presently being employed for such diverse functions as weather forecasting, aircraft design, missile control, language translation experiments, production regulation, specialized records storage, and the integration of the aircraft warning net. The common denominator of all these activities is the processing of large amounts of information. The expanding interest of scientists generally in the potentialities of these devices has in recent years begun to extend into the ranks of biological scientists, who have started to explore the possibilities inherent in computers for the versatile handling of large quantities of complex data. This article will review some of the first pioneering applications of these machines to medicine and biology and suggest some of the future pathways along which further applications may be found.

Characteristics of Computers

The almost limitless horizon for the scientific use of computers stems from the following basic considerations. Any problem in logic which can be stated in mathematical symbols, even if the resulting expression is very complex, can actually be solved by reducing it to a series of simple combinations of the four basic operations of arithmetic. Needless to say, this breakdown normally results in an enormous expansion in the number of mathematical operations finally needed to achieve a quantitative result, even though each operation is simple arithmetic. However, it is precisely this transformation which permits the application of the unique features of a computer to the solution of complex scientific problems stated mathematically, since the primary advantage of these devices is their ability to perform amazing numbers of arithmetic procedures in a small fraction of the time which would be necessary by hand computational or desk calculator methods.

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As a preliminary step in studying the biological applications of computers, we will examine the two basic types of computers in use today. These can be classified broadly into the analog and digital types. This division arises according to the way in which the numbers, on which the machine operates, are represented in it. In the analog machine, numbers are represented by physical phenomena which can be varied, such as pressures, forces, and angles. Computations or operations are then carried out comparing these representative numbers or analogs. These computers are employed to find some phenomenon which parallels in behavior the continuous parameters of a particular system, be it biological or physical. The analog computer is really a physical measuring device, of which a simple example is the slide rule, where the analog is scalar distance and where operations are carried out through adding, subtracting, and comparing these distances. The basic operations of the analog machine include the four conventional species of arithmetic plus the more esoteric operations made possible by the use of a differential analyzer. By "programming" a computer is meant the means whereby the arithmetic procedures which are to replace the complex higher mathematical formulas are scheduled into the computer in a correct sequence.

Although the basic operations of digital machines are also based on simple arithmetic, they cannot deal with approximations as an analog computer can, but only in coded, fixed choices. The programming of an elaborate switching procedure enables the computer to handle progressively more complex mathematical operations as it extends the number of choices it can make. Therefore, digital computers must work on discrete numbers. These machines are capable not only of performing simple arithmetic at incredible speeds but also of storing and recalling immense quantities of information based on the retrieval by the machine of a stored code in response to an appropriate signal. Digital devices can process vast amounts of data to accomplish routine operations as required in industry for payroll or record purposes or they can perform a multitude of mathematical operations for the analysis of a particular system as required in the sciences.

Both analog and digital computers can deal with abstract models of a particular system. The main limitation of analog machines relates to precision. Precision of analog machines is limited by the accuracy with which the physical analog being employed can be measured. Digital machines, however, can achieve any desired precision and that with relative facility.

The increasing use of mathematical concepts such as curve fitting, probability theory, advanced statistics, and model construction in biology and medicine has created an urgent need for a means of handling the masses of data and higher mathematical techniques in a rapid fashion. The coincidental arrival of the biological sciences and of computer technology at their present high level of scientific capability presents both fields with an opportunity to combine their techniques in a systematic search for solutions to problems which have not yielded to traditional methods. Computers certainly would not have found any application in the traditional descriptive approach to biology.

Air Force Interest in Computers

A series of recent regional conferences between representatives from the fields of computer technology and the medical sciences for the purpose of exploring the applications of modern automatic data processing devices to medicine and biology have been sponsored by the Air Force's Air Research and Development Command (ARDC).[1] The investment by the Air Force of major amounts of national resources for the advancement of computer theory and technology has led to a conviction in the ARDC that it had an obligation to acquaint the civilian scientific community with information developed for military purposes which would also contribute to the general body of scientific knowledge. The Air Force has also been keenly aware of the fact that public funds spent for defense could accrue scientific side-benefits that might have more lasting effect and application than some of the computer monitored weapons it has today.

At the ARDC conferences members generally agreed that increasing application of computer techniques would be made in both the medical and biological sciences. Both Dr. George Thorn, professor of medicine, and Dr. Bert Vallee, associate professor of medicine, at Harvard University, strongly voiced the need for further pioneering studies of basic model systems prior to the application of computer techniques to clinical medicine. A positive suggestion that a national computer facility be established to which smaller biological centers could turn was conveyed to the Cambridge conference by Dr. George Karreman as the proposal of Dr. Albert Szent-Gyorgyi, director of the Institute of Muscle Research, Marine Biological Laboratory at Woods Hole. Dr. Howard Aiken, one of the original pioneers in the development of computers and presently director of the Harvard Computation Laboratory, stressed the urgent need for cross-training individuals in a number of disciplines including medicine in order to enable them to think most productively in this new interdisciplinary area. He even suggested a modified residency program in computer techniques for qualified physicians.

These conferences disclosed that some computer techniques are already being applied to medical problems. Dr. Rufus Hessberg described at one of the conferences the development of an automatic electroencephalogram analyzer at the Aero Medical Laboratory of the Wright Air Development Center.

The electroencephalogram is a wave pattern which represents the electric potentials from the brain as recorded by electrodes attached to the scalp. The amplitude and frequency of these waves are electrical quantities which can be fed into and automatically analyzed by an analog computer. An elaboration of this device has been constructed by Dr. Neil Burch of Baylor University, who initiated the development previously mentioned at the Aero Medical Laboratory.[2] Similarly, the analysis of any of the bioelectrical phenomena such as the electroretinogram, electrocardiogram, electromyogram, cochlear microphonics, galvanic skin responses, action potentials, unicellular potentials for both clinical and research applications could all be performed by specialized automatic data processing devices.

Dr. John Womersley, also of the Wright Air Development Center, has evolved a model of the hemodynamic forces present in the larger arteries.[3] The mathematical problem is that of the relation between the oscillatory properties of an elastic container and a liquid of uniform viscosity which is propelled by an intermittently applied force against a constant resistance. The relation of these forces can be described by a formula, the validity of which has to be checked by varying the functions with respect to each other to determine the full range of variability and by correlating these with a few experimental observations. Dr. Womersley, in order to integrate these variables into a mathematical formula which could be employed as a physiological model, depended to a great extent on computers.

This example suggests two important areas of computer application. One is the obvious speeding up of involved mathematical calculation which may be inherent to a particular biological problem. The other is the construction of special circuitry which will cause electrical functions to vary with respect to each other in the same mathematical relationship as the biological functions. In this manner, simulation of a biological system by an electrical system is achieved. We see then that, by means of mathematical formulations, biological processes, whether on a molecular, cellular, organ system, or total organism level, can be duplicated in much the same way that aerodynamic characteristics of new or proposed aircraft are simulated by computers. For example, a computer designed to simulate thermoregulatory mechanisms or homeostasis must have the variables in that process defined in terms of numbers.

Computers in Statistical Operations

Where the problem involved amounts basically to solving mathematical equations or carrying out lengthy statistical calculations as may be required during mass standardization studies of drugs, toxins, and vaccines, the presently available computers would be widely applicable. Several examples of computer application of this kind have already been made in both preventive and clinical medicine, particularly with problems wherein there exists a need to correlate vast amounts of data. In the field of public health and preventive medicine, this application has greatly speeded correlation analyses and made possible the solution of complex epidemiologic problems. The evaluation of the effectiveness of the Salk vaccine,[4] the current studies relating tobacco and cancer, and tobacco and cardiovascular disease have been greatly aided by the use of automatic data processing machinery and computers in complex statistical procedures. The number of these applications is limited only by the facilities available.

There are many such facets to the application of computers to clinical medicine. Computers can, for example, be applied in much the same manner as above for the evaluation of clinical laboratory procedures, for determining the efficacy of drugs, and for speeding the solving of correlation problems. At the Chicago conference, Dr. Sam Swartz, of the University of Minnesota's department of experimental medicine, reported his investigations, employing computer techniques, into the relative value of liver function tests in a number of diseases. His preliminary data suggest that only four tests have independent value and that performing more is superfluous. The correlation of the clinical tests and variables of a particular disease both for their prognostic value and for the evaluation of the efficacy of different therapies is another example of the type of correlation problem that can be rapidly handled by existing computers. These techniques could, for example, be employed in a relative study of the treatments of acute barbiturate intoxication or diabetic acidosis. Likewise, studies on the correlation between the degenerative diseases and such factors as race, age, or sex, or the correlation between suspected predisposing conditions and cancer (as for example, between biliary stasis and hepatic carcinoma) can be greatly speeded by computers.

The analysis of complex clinical investigations can also be speeded by computers, particularly those in psychiatry, where numerous objective and subjective measurements are obtained which can accumulate into vast amounts of data within a short time. A study of this type was reported at the Los Angeles conference by Dr. Eli Robins of the department of psychiatry of Washington University. He is correlating the childhood and adult personalities of 525 people with the aid of a computer in order to identify prognostic variables.

Automatic Data Handling

Another sort of application is to be found in the design of specialized computers for specific tasks. These computers are not always of the large scale category. The Air Force has, for example, developed many small computers for in-flight use that aid in solving the specific geometric and trigonometric problems involved in navigation and bombing. The clinical application of small scale computers and the integration of computer techniques into medical instrumentation is also already in progress. For example, automation of routine clinical laboratory procedures is currently under way. Many clinical laboratory procedures depend on colorimetric end-points for interpretations. The conversion of these into electrical measurements is feasible. They can then be analyzed by a specialized small computer with increased speed and greater accuracy. Certain long-term therapeutic devices and techniques definitely require some degree of automation. Present mechanical breathing devices, for example, do little to prevent disuse atrophy of viable tissues. Dr. Elliot Newman, professor of medicine at the Vanderbilt Medical Center, reported at one of the conferences the development of a respiratory calculator, sensitive to bursts of voluntary activity and to the carbon dioxide content of exhaled breath. It will automatically encourage normal mechanisms by reciprocally decreasing the activity of the respirator.

Several attempts at applying computers to facilitate the solution of both research and clinical problems in cardiopulmonary studies and neurophysiology have been made. Both cardiac and pulmonary function tests frequently require considerable mathematical calculations between each step. This makes these tests both lengthy and expensive. Automatic devices can perform this task smoothly and economically. Several such devices have been developed. Gelfand and Lambertsen of the University of Pennsylvania have constructed an instantaneous respiratory minute volume computer. Kubicek, of the University of Minnesota, has developed a computer for the continuous recording of oxygen consumption rate and oxygen and carbon dioxide concentration in the expired air of human subjects. To improve the clinical value of the blood volume determinations, Dr. Newman has constructed a special computer which simulates time concentration curves after the injection of a dye into the circulation. He has also employed a computer to integrate the information obtained from various electrocardiographic leads into a three dimensional expression possessing both form and direction in order to improve the diagnostic value of vector spatial electrocardiography.[5] By applying feed-back concepts in his experimental investigations into vector electrocardiography, Dr. Otto Schmitt[6] related at the Chicago ARDC conference how with the aid of a computer he has been able to suggest biological servo-mechanisms to account for certain features of the vector arrangements.[7] Such use of computers enables the concurrent manipulation of the variables of a particular situation and permits continuous analysis. For example, the use of the computer to integrate results of a continuous analysis of arteriovenous oxygen differences and oxygen consumption was recently reported at a meeting of the Southern Society for Clinical Research. It is possible to determine the cardiac output on this computer continuously.

In the field of neurophysiology the work of Dr. Warren McCulloch of the Massachusetts Institute of Technology may be mentioned. At the conference held in Cambridge, he suggested the use of computers to aid in the localization of functional centers within the central nervous system. Rosenblith and Barlow of MIT have employed computers in their application of autocorrelation analysis to electroencephalography. Dr. Arthur Ward of the University of Washington told at the ARDC conference in Los Angeles how he has used a computer to process data obtained from action potentials recorded from the motor cortex during neurosurgical operations. The amplitude, duration, and latency of the action potential are among the quantitative variables programmed into his computer.

Another category of computer application stems from its ability to store and to recall quickly immense quantities of information. The tremendous amount of data recorded on hospital charts or in the journals suggests two possible applications of great practical value; the sheer mass of this material is so staggering that it defies efforts at retrieval. While the practical problems involved in designing and building data holding capacity adequate for this task into computer facilities of reasonable size and cost have not yet been solved, their use as information storage devices might well, in the future, facilitate the recall of data in a manner far surpassing in speed and thoroughness any present methods. Data processing devices with their high speed reaction time and infallible memory can probably be built to pull out any properly and distinctly coded item or category of items occurring in a hospital's entire experience in less time than is usually required to find one complete case history. In this way all of the information pertinent to any specific variable or relationship under investigation could be made available, a feat hardly even possible at this time without the expenditure of enormous effort.

Simulation of Biological Processes

The application of computers to medical and biological problems often involves construction of special duplicating circuitry which simulates particular conditions. Computer technology is being advanced currently to achieve solution of the more complex problems which may involve not only simulation circuitry but also new concepts in switching and information theory. Several examples of this type of application can be cited. A number of special computers have been constructed to simulate various enzyme systems. Berman and Schoenfeld of the Sloan-Kettering Institute have reported one such instance in their formulation of biological models of enzyme systems. They have employed radioactive isotopes as trace elements in this technique. Dr. Britton Chance of the Johnson Foundation has also reported on the use of a computer in his investigations into enzymology.[8]

There is real and widespread interest in future possibilities of the model type application. At least three types of such application are envisioned. The first involves a model of a system whose parameters are readily determinable. An example of this is Dr. Womersley's model which has previously been described.

A second type of model is one in which a system is statistical rather than determinate. In this case we have definite concepts of how the functions of a particular system vary with respect to each other. However, their interactions are within statistical distributions. Statistical quantum mechanics illustrates this type of system as the parameters of subatomic particles such as velocity or location can be stated only in terms of statistical ranges. This type of model could be applied in elucidating the epidemiology of a disease such as atherosclerosis about which a number of statistical factors are known.

The third type occurs in conditions when the structure is unknown and when we do not have a preconceived concept of the model. Here computers could be employed to explore a group of hypotheses to help in selecting the most likely, thereby narrowing down the number of possibilities for which experimental verification need be sought. In this manner the structure of a model is postulated. Although the implication here is that a machine would perform some of the scientist's intellectual work, it is mainly the intuition and judgment of the expert which can make possible the construction of any particular model of a hypothesis. Very often biological problems involve theoretical concepts whose parameters are poorly defined. For example, in attempting to explain the electrophysiology of the cell membrane, it may be advantageous to manipulate various parameters to gain insight into possible patterns of structure and function. Pepinsky of the Pennsylvania State College has constructed a special computer designed to aid in elucidating the complex molecular structure of proteins.

Several mathematical techniques may be utilized to aid in the application of computers to biological problems of the second and third types, which represent perhaps the most stimulating kinds of application. Dr. Anthony Bartholomay, mathematical biologist at Harvard University, has, for example, employed Wald's theory in describing medical phenomena.[9] This theory is based on the concept of sequential procedures combined with the loss function for faulty judgments. It is the basis for a unified theory of experimentation and statistical decision-making. Another technique is the Monte Carlo method.[10] This technique is a means of approximating mathematically a formula which cannot be stated in its finite form because of the complexity of the system that it represents. At the Chicago conference, Dr. George Gamow of the University of Colorado explained the use of this method, both to analyze the structure of proteins and to suggest the probable interactions between amino acids, peptides, and peptones during the synthesis of proteins. Similar uses of this method have been reported by Hoffman and Metropolis of the National Institutes of Health in their investigations into morphology.[11]

It is likely, as John von Neumann [12] has indicated, that mathematicians can aid in explaining the functional structure of the nervous system and be benefited by recognition of other patterns of logic, which could lead to the development of new types of circuitry. Basically, von Neumann has postulated that the nervous system employs a radically different system of notation from that of mathematics. Instead of the precise systems of computers, the nervous system employs a system of notation in which the meaning of a volley of impulses is deduced from the fact that it falls within a statistical range of volleys all of which convey qualitatively the same message. Thus, if a single pulse is lost in a computer, the obtained solutions are completely nonsensical. In the nervous system, pulses are frequently lost without distorting the meaning of a particular message. An understanding of the statistical method of symbolic notation employed by the nervous system to transmit information could lead to wholly new and unconventional computer concepts.

Growth of National Interest

Because of the increasingly frequent employment of quantitative methods and mathematical techniques in medicine and biology, other organizations such as the National Institutes of Health, the National Biophysics Association, and the Institute of Radio Engineers have held meetings between representatives of the medical sciences and computer technology. Similar in scope to the Air Force conferences, these meetings have acquainted prominent authorities with the potentialities of computers in medicine and have helped to overcome barriers of language and viewpoint which exist between the several disciplines. At one such recent meeting held at NIH in May, 1958, Eden and Noble discussed the development of an analog computer for the analysis of experimental distribution curves.

Many types of computers are available today. The ease of their adaptability has been suggested. The interest shown by medical and biological scientists at all these conferences attests to the fact that computers will play an increasingly important role. Recognizing this fact, the National Academy of Sciences–National Research Council with Air Force and NIH support have appointed a group to consider the applications of computers to medicine and biology. It will analyze the types of medical and biological problems in which computers have been employed and will recommend the types of situations to which they could profitably be applied. Their recommendations will serve to familiarize biologists and medical scientists with the capabilities and potentialities of computers. By this means original workers will be alerted to the possible applications of these new tools in their own fields of endeavor. The long-term result of all this activity to the great satisfaction of the nation as well as the Air Force could be that the immense amount of funds poured into the development of defensive weapons would in the end also earn important dividends for the healing arts and the biological sciences.

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HYPONATREMIA IN CONGESTIVE HEART FAILURE.—Acute intensification of chronic congestive failure in cardiac patients on low sodium diets may lead to continued water retention, with increasing edema and hyponatremia without external loss of sodium. This sequence is illustrated by the events following development of severe respiratory infections or escape from digitalization in such patients. Such a sequence may occur also, at times, in the presence of electrocardiographic changes suggestive of digitalis toxicity but actually due to potassium depletion. This clinical course is not favorably influenced by intravenous administration of either isotonic or concentrated sodium solutions. However, increasing cardiac output by adequate digitalization or decreasing bodily metabolic demand by treatment of the underlying infection may lead to increased excretion of water in excess of sodium, decreased body weight, and restoration of more normal serum electrolyte concentrations. This sequence of events is attributed to sustained production of antidiuretic hormone, invoked by some extraosmoreceptor mechanism, whenever the cardiac output becomes inadequate for the body's metabolic needs. The more protracted operation of this mechanism is illustrated by the progressive water retention and hyponatremia frequently observed in patients on a low sodium diet and unrestricted water intake during the terminal phase of congestive failure. A fatal outcome may be anticipated unless the cardiac output can be increased or the burden on the impaired circulation in some way diminished.—R. E. Weston, M.D., Ph.D., J. Grossman, M.D., E. R. Borun, M.D., The Pathogenesis and Treatment of Hyponatremia in Congestive Heart Failure, *The American Journal of Medicine*, October, 1958.

LACTATION INHIBITION BY DELADUMONE INJECTED DURING LABOR OR JUST AFTER DELIVERY

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The course of postpartum changes in the breast was followed in 310 women who did not wish to breast feed their infants. A hormone preparation containing 90 mg. of testosterone enanthate and 4 mg. of estradiol valerate per cubic centimeter was injected parenterally in a single dose in each of 185 patients. These were compared with 83 patients who received a somewhat similar androgen-estrogen preparation in repeated doses by mouth and 42 who did not receive any hormone medication. Each patient was classified with respect to postpartum enlargement of breasts, signs of discomfort, and requirements of treatment with aspirin, binders, or ice caps. The incidence of engorgement among 268 hormone-treated patients was 8.3% as compared with 69% among 42 patients not so treated, and an equally marked difference was found in regard to postpartum breast pain. The parenteral medication, when injected in doses of 3 or 4 cc., was more effective than the oral medication, and a study of dosages and timing led to the conclusion that the most effective dosage of the parenteral preparation was a single injection of at least 3 cc. given preferably within the first hour post partum or at the end of the first stage of labor.

Postpartum breast engorgement in the nonnursing mother is one of the most common minor problems of the obstetrician. Although a large number of studies demonstrate the inhibition of lactation by estrogens and/or androgens,[1] the clinical results have not always been as successful as desired.

The study reported here was undertaken to evaluate the lactation-inhibiting efficacy and the possible undesirable actions of a single injection of a long-acting androgen-estrogen combination. The preparation, Deladumone, contains 90 mg. of testosterone enanthate and 4 mg. of estradiol valerate per cubic centimeter of sesame oil in true solution. Prior to development of this agent for parenteral administration, we had utilized several hormone preparations for the control of postpartum breast manifestations, and on the basis of clinical impressions we had been satisfied, in general, with a short-acting androgen-estrogen preparation for oral administration (Tylosterone) containing 5 mg. of methyltestosterone and 0.25 mg. of diethylstilbestrol per tablet. This was administered in a dosage of one tablet three times a day during the hospital stay (five to six days) beginning shortly (two to eight hours) after delivery. Therefore, we compared the results that we obtained with the new parenterally given preparation with those we had achieved with this orally given medicament.

Plan of Study

The investigation concerns 257 private patients who did not wish to nurse. They were divided into three main series: Series 1 was a control group of 42 patients (group 1) who did not receive any medication. Series 2 consisted of 83 patients (group 2) who received the orally given androgen-estrogen preparation as described above. Series 3 consisted of 132 patients who were given parenterally the androgen-estrogen preparation. As the study progressed, series 3 was subdivided into groups 3 through 7 on a basis of dosage and interval of elapsed time between delivery and injection as follows: group 3: 27 patients, 2 cc. given ½ to 8 hours post partum; 4: 55 patients, 3 cc. given ½ to 8 hours post partum; 5: 10 patients, 2 cc. given ⅓ to ⅔ hours post partum; 6: 22 patients, 3 cc. given ⅓ to ⅔ hours post partum; 7: 18 patients, 4 cc. given ⅓ to ⅔ hours post partum.

Each of the patients was visited by one of us daily during her hospitalization (usually five to six days), and her clinical status during this period was classified as follows: grade 0, neither the patient nor the doctor noted breast engorgement or discomfort; grade 1, either the doctor or the patient noted enlargement of the breasts, but pain was not present; grade 2, the patient complained of mild pain which did not require treatment with analgesics; some engorgement always was present, but varied with the individual; grade 3, engorgement was present and the amount of pain necessitated treatment with aspirin and/or breast binder and/or ice caps; grade 4, engorgement was pronounced and codeine was required in addition to the other measures.

Results

The results of these varied therapeutic regimens are presented in tables 1 to 5. As would be expected, the 42 untreated patients (group 1) had a high incidence of breast engorgement with 69% requiring analgesia. In contrast, only 8.4% required analgesia and 21.7% experienced slight discomfort in the group of orally treated patients (group 2).

Table 1.—*Effectiveness of Different Courses of Steroid Therapy in Preventing Postpartum Breast Manifestations in 257 Cases During Five Days of Hospitalization*

				No of Cases with Breast Manifestations, Grouped by Grade									
				0		1		2		3		4	
Group, No.	No. of Cases	Steroid Hormone Preparation	Dosage	No.	%	No.	%	No.	%	No.	%	No.	%
			No Treatment										
1	42	None	...	1	2.4	2	4.8	10	23.8	18	42.8	11	26.2
2	83	Tylosterone	Given ½ to 8 Hr. After Delivery										
3	27	Deladumone	1 tablet, 3 times a day	36	43.4	22	26.5	18	21.7	7	8.4	0	0
4	55	Deladumone	2 cc.	5	18.7	6	22.5	8	29.9	8	29.9	0	0
			3 cc.	29	52.7	19	34.6	7	12.7	0	0	0	0
Given ⅓ to ⅔ Hr. After Delivery													
5	10	Deladumone	2 cc.	3	30	2	20	3	30	2	20	0	0
6	22	Deladumone	3 cc.	13	59.1	6	27.3	3	13.6	0	0	0	0
7	18	Deladumone	4 cc.	12	66.7	4	22.2	2	11.1	0	0	0	0

The women treated with 2 cc. of Deladumone (group 3) exhibited improvement over the untreated patients (group 1), but the results were not impressive, with 29.9% requiring analgesia. Consequently, the dosage employed was increased and the patients given 3 cc. of Deladumone (group 4) were evaluated. In this group, none of the 55 patients required analgesics and only 12.7% complained of slight pain. As this group was being studied, the response at first seemed to be spectacularly good, but then cases of breast discomfort began to appear. Investigation disclosed that, because of an exceptionally large patient load, the nursing staff had not been able to give the Deladumone until two to eight hours after delivery. This suggested that a delay in the administration of the Deladumone might affect the response. Therefore, the effect of an immediate postpartum injection was investigated. Initially, a group of patients was given 2 cc. (group 5), and the response proved to be somewhat better than that in group 3 (20% compared with 29.9% requiring analgesia), where the same dosage had been employed without regard to timing, although in the majority of cases the injection was given within the first hour post partum. However, the response from the 2-cc. injection immediately post partum (group 5) was not as good as that obtained with the 3-cc. dosage in group 4.

Table 2.—*Effect of Route of Administration and of Time of Starting Therapy on Effectiveness of Hormone Treatment in Prevention of Postpartum Breast Engorgement*

		Cases of Engorgement		
			Significant,	
Route, Dosage, and Administration	No. of Cases	Insignificant, No.*	No.†	%
No hormone treatment	42	13	29	69.0
Tylosterone	83	76	7	8.4
Deladumone				
Delayed after delivery (½ to 8 hr.)				
2 cc.	27	19	8	3.0
3 cc.	55	55	0	0
At once after delivery (⅓ to ⅔ hr.)				
2 cc.	10	8	2	20.0
3 cc.	22	22	0	0
4 cc.	18	18	0	0
All parenteral treatment	132	122	10	7.6
All hormone treatment	215	198	17	7.9

* Cases in grades 0, 1, and 2 of table 1 combined.
† Cases in grades 3 and 4 of table 1 combined.

Group 6 then was evaluated in order to find out whether an immediate postpartum injection of 3 cc. of Deladumone would produce a more favorable response than that in group 4. The results were nearly the same. The next step was to test the effect of a still larger dose, i. e., 4 cc. of Deladumone given immediately post partum in an attempt to eliminate breast engorgement altogether. In this small group of 18 patients (group 7), the injection was administered uniformly one-third to two-thirds hours after delivery. The results were slightly better than in the series of patients given 3 cc. (group 6)—22.2% compared to 27.3% grade 1 reactions, and 11.1% compared to 22.2% grade 2 reactions; all of the remaining cases in both groups being grade 0.

Table 3.—*Effect of Route of Administration and of Time of Starting Therapy on Effectiveness of Hormone Treatment in Prevention of Postpartum Breast Pain*

			Cases with Varying Degrees of Pain†	
Route, Dosage, and Administration	No. of Cases	Cases with No Pain, No.*	No.	%
No hormone treatment	42	3	39	92.9
Tylosterone	83	58	25	30.1
Deladumone				
Delayed after delivery (½ to 8 hr.)				
2 cc.	27	11	16	59.3
3 cc.	55	48	7	12.7
At once after delivery (⅓ to ⅔ hr.)				
2 cc.	10	5	5	50.0
3 cc.	22	19	3	13.6
4 cc.	18	16	2	11.1
All parenteral treatment	132	99	33	25.0
All hormone treatment	215	157	58	27.0

* Cases in grades 0 and 1 of table 1 combined.
† Cases in grades 2, 3, and 4 of table 1 combined.

Undesirable manifestations occurred with both the oral and the parenteral medication. The chief difficulty with the orally given preparation as used in this study was the tendency for breast engorgement of varying degrees to occur after cessation of the therapy. Unfortunately, the exact incidence of this difficulty was not tabulated, but it is our clinical impression that the incidence was about 5%. The only other undesirable effect of Tylosterone was the occasional occurrence of edema, a manifestation based on clinical observation rather than measurement.

Table 4.—*Effect of Route of Administration and Amount of Medication on Effectiveness of Hormone Treatment in Prevention of Postpartum Breast Engorgement*

Route, Dosage, and Administration	No. of Cases	Cases of Engorgement: Insignificant, No.*	Cases of Engorgement: Significant, No.†	Cases of Engorgement: Significant, %
No hormone treatment	42	13	29	69.0
Tylosterone	83	76	7	8.4
Deladumone				
2 cc.	37	27	10	27.0
3 cc.	77	77	0	0
4 cc.	18	18	0	0
All parenteral treatment	132	122	10	7.5
All hormone treatment	215	198	17	7.9

* Cases in grades 0, 1, and 2 of table 1 combined.
† Cases in grades 3 and 4 of table 1 combined.

Delayed engorgement of the breasts, after the discharge of the patient from the hospital as described above with the oral medication, did not occur in the study with Deladumone. However, 5 patients (3.8%) of the 132 who received Deladumone had slight to moderate reddening and swelling at the site of the injection. No serious reactions were encountered. One of the patients with a local reaction had a delayed postpartum hemorrhage, and on curettage no retained placental tissue was found. No edema or undesirable androgenic effects were observed. One patient who had received 3 cc. of Deladumone changed her mind about nursing, and was able to nurse successfully.

Summary and Conclusions

In any study such as this, subjective factors play a considerable role. The observer is influenced by what he thinks is normal, by what he expects or desires to think, and by his own attitude toward pain. The variations and vagaries of each patient's "threshold of pain" are too intangible to measure. In spite of these difficulties, we have attempted to evaluate the efficacy of a single dose of the parenterally given, long-acting androgen-estrogen preparation, Deladumone, for the control of postpartum breast engorgement and pain. From a study of 257 patients treated with various therapeutic regimens (42 with no medication, 83 with an oral androgen-estrogen medication, and 132 with single injections of Deladumone), we have reached the following conclusions concerning Deladumone: 1. The preparation is safe. The only undesirable effect that developed was a slight to moderate local reaction at the site of the injection occurring five times (3.8%) in 132 cases. 2. The preparation is effective. When employed in an adequate dosage at the proper time, the need for analgesics to control the breast symptoms is practically eliminated. None of the 95 patients thus treated required analgesics, and only 12 (12.6%) complained of very mild symptoms of pain or discomfort. In contrast, 7 (8.4%) of 83 patients treated with an oral androgen-estrogen regimen required analgesics, and 18 additional patients (21.7%) complained of some discomfort. Thus, Deladumone was more effective than the oral medication regimen evaluated in this investigation. 3. The most effective dosage of Deladumone is at least 3 cc. as a single injection. 4. The injection of Deladumone should be given as soon as possible after delivery, preferably within the first hour post partum. 5. The use of a single injection of Deladumone is more convenient and less time-consuming for the patient and the nursing personnel than the repeated administration of oral medication. 6. The use of Deladumone appears to essentially eliminate the undesirable withdrawal reaction or secondary breast engorgement that occasionally follows the cessation of oral medication.

Addendum

Since this report was prepared, we have continued to use Deladumone on our private patients. Group 7 has been increased to 48 patients who were given 4 cc. one-third to two-third hours post partum. In the 48 cases, the breast manifestations (table 1) were classified as grade 0 in 26 (54.2%), grade 1 in 15 (31.2%), grade 2 in 3 (6.2%), grade 3 in 2 (4.2%), and grade 4 in 2 (4.2%). Engorgement (table 2) was insignificant in 44 and significant in only 4 (8.3%). Pain (table 3) was absent in 41 and present in varying degrees in only 7 (14.6%).

In addition, the effect of 4 cc. of Deladumone given at the end of the first stage of labor was evaluated in 23 women (group 8). In these 23 patients, the breast manifestations were classified (table 1) as grade 0 in 14 (60.9%), grade 1 in 6 (26.1%), grade 2 in 2 (8.7%), grade 3 in 1 (4.3%), and grade 4 in none. Engorgement (table 2) was insignificant in 22 and significant in only one (4.3%). Pain (table 3) was absent in 20 and present in varying degrees in only 3 (13.0%). Thus, the results were slightly better than in the series of patients given 4 cc. immediately post partum (group 7)—60.9% compared to 54.2% grade 0

Table 5.—*Effect of Route of Administration and Amount of Medication on Effectiveness of Hormone Treatment in Prevention of Postpartum Breast Pain*

Route, Dosage, and Administration	No. of Cases	Cases with No Pain, No.*	Cases with Varying Degree of Pain†: No.	Cases with Varying Degree of Pain†: %
No hormone treatment	42	3	39	92.9
Tylosterone	83	58	25	30.1
Deladumone				
2 cc.	37	16	21	56.7
3 cc.	77	67	10	13.0
4 cc.	18	16	2	11.1
All parenteral treatment	132	99	33	25.0
All hormone treatment	215	157	58	27.0

* Cases in grades 0 and 1 of table 1 combined.
† Cases in grades 2, 3, and 4 of table 1 combined.

reactions, 26.1% compared to 31.2% grade 1 reactions, 8.7% compared to 6.2% grade 2 reactions, 4.3% compared to 4.2% grade 3 reactions, and 0% compared to 4.2% grade 4 reactions. The injection of Deladumone at the end of the first stage had no effect on the subsequent course of the labor.

With the additional cases, a total of 268 women have been treated with hormone preparations. In these, breast engorgement (table 4) was insignificant in 246 and significant in 22 (8.3%); pain (table 5) was absent in 202 and present in varying degrees in 66 (24.6%). Including the additional cases, we have administered Deladumone to 185 women. In these, breast engorgement (table 2) was insignificant in 170 and significant in only 15 (8.2%); pain (table 3) was absent in 144 and present in varying degrees in 41 (22.2%). A dose of 4 cc. has been administered to 71 patients. In these, breast engorgement (table 4) was insignificant in 66 and significant in only 5 (7.0%); pain (table 5) was absent in 61 and present in varying degrees in 10 (14.1%). Of the 185 women who received Deladumore, 7 patients (3.8%) had slight to moderate reddening and swelling at the site of injection. Only 4 (4.8%) of the 125 patients treated with an adequate dose at the proper time required analgesics, and only 13 (10.4%) complained of very mild symptoms of pain or discomfort. No serious reaction of any kind has occurred.

Our continuing experience supports our previous conclusion that Deladumone is safe and is more effective than the oral medication evaluated in this investigation. The effective dosage of Deladumone is at least 3 cc.; it should be administered immediately after delivery. Furthermore, the injection may be given at the end of the first stage of labor. When thus administered, Deladumone does not alter the subsequent course of the delivery and appears to be slightly more effective in controlling the breast manifestations.

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The long-acting androgen-estrogen combination used in this study was supplied as Deladumone by E. R. Squibb & Sons, New York; the short-acting androgen-estrogen preparation was supplied as Tylosterone by Eli Lilly & Company, Indianapolis.

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BAGGY EYELIDS.—The title, "Baggy Eyelids," may not be representative of scientific terminology, but it does express in the patient's own words, exactly what it is that bothers him, and for which he seeks relief. What causes bagginess of the eyelids? People free from this complaint are wont to charge its possessor with orgies of dissipation, and debauchery in all directions, when actually most of the sufferers may lead an exemplary and hygienic life. Nor have eyestrain, kidney trouble, thyroid deficiency or allergy any but the rarest connection with it. The actual cause in an inheritable family tendency toward over-development of otherwise perfectly normal intraorbital fat, with the result that some of this fat bulges or herniates forward into the area between the eyeball and eyelid, thereby causing the bagginess. . . . Baggy eyelids, . . . is suffered by its owner, because he knows that it runs in the family, hence [he thinks] nothing can or should be done to correct such a disfigurement. A technique is presented which overcomes this embarrassing complaint . . . [by] 1. Removal of the excessive amount of fat, i. e., the contents of the bags. 2. Removal of the stretched redundant skin, which forms the bag.—H. O. Bames, M.D., Baggy Eyelids, *Plastic and Reconstructive Surgery*, September, 1958.

PREVENTION OF POSTPARTUM LACTATION BY ADMINISTRATION OF DELADUMONE DURING LABOR

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and
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Inhibition of postpartum lactation was accomplished in 197 women by single intramuscular injections of a preparation containing 90 mg. of testosterone enanthate and 4 mg. of estradiol valerate per cubic centimeter of sesame oil. Four modes of administration were compared. The least effective of the four consisted of administering 2 cc. immediately or within two hours after delivery; it rendered 22 (43%) of 51 patients completely free from such complaints as breast pain or fulness. The most effective was a dose of 3 cc. given after the first stage of labor; it rendered 43 (92%) of 47 patients completely asymptomatic. The dosages did not exceed 3 cc., and there was no evidence that they affected the course of labor, interfered with postpartum physiological adjustments, or induced bleeding or masculinization in any patient. Inhibition of lactation by this combination of hormones was overcome, in two instances, when women decided to breast feed their infants and placed them to the breast. Although the suckling stimulus readily overcame the hormone-induced inhibition, this medication was evidently more effective than the classic procedures of fluid limitation, breast binders, diuretics, ice packs, and sedation.

The prevention of postpartum lactation and breast engorgement has become an increasingly important problem in medical practice during recent years because of the modern trend away from the breast feeding of newborn infants which has developed from a combination of economic, social, and personal factors. The classic therapeutic procedures (fluid limitation, breast binders, diuretics, and the use of ice packs or sedation) rarely are sufficient to eliminate the discomfort or the prolonged periods of milk leakage. Inhibition of the anterior pituitary gland production of the lactogenic hormone with hormone therapy has been more effective. However, estrogens alone[1] may stimulate endometrial proliferation, retard normal involution of the uterus, and be followed by secondary breast engorgement and/or uterine bleeding; androgens alone[2] may interfere with the involution in the uterus and the onset of normal menses. In contrast, a more favorable response has been reported after administration of androgen-estrogen combinations,[3] and a combination of a long-acting androgen with a long-acting estrogen appeared to be particularly advantageous.[4] All types of hormone therapy appear to be ineffective, however, unless treatment is instituted within a few hours of delivery and all suckling is avoided.

When a long-acting androgen-estrogen combination for parenteral administration became available, a study was undertaken to determine whether the patient would receive greater benefits from hormones administered early in the course of labor. The preparation used, Deladumone, is an optimally balanced, long-acting combination of esters of the naturally occurring testicular and follicular hormones, testosterone enanthate and estradiol valerate, in clear solution of low viscosity which readily can be injected through a small-gauge needle. It contains 90 mg. of testosterone enanthate and 4 mg. of estradiol valerate per cubic centimeter of sesame oil.

Method of Study

A total of 197 women in a private hospital obstetric service were treated with Deladumone in this investigation. The patients were not selected for age, parity, or previous nursing experience and included both primiparous and multiparous individuals. These women either did not desire or were physically unable to nurse their babies. The cases consisted of four clinical groups, as given in the table.

The Deladumone was administered as a single intramuscular injection. In the postpartum period, the patients continued to take a routine diet and liquids and were examined daily during the five or six days of hospitalization. The efficacy of the hormone therapy was evaluated from the subjective symptomatology and the objective physical findings, with particular attention to the occurrence of pain, fulness, or other significant breast changes, and to the incidence of bleeding, or of signs of masculinization (such as voice changes or hirsutism). The majority of the patients were followed after discharge for approximately two months to evaluate the incidence of secondary engorgement,

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From the gynecologic and obstetric services, St. John's Episcopal Hospital.

change in the nature of the lochia, uterine bleeding, decrease in the rate of uterine involution, or delay in the onset of normal cyclic ovarian function.

Results

The results obtained in this investigation with Deladumone as hormonal therapy for postpartum breast management of non-nursing mothers indicate that the preparation is most effective in preventing lactation when administered as a single 3-cc. injection immediately after the first stage of labor (see table). The administration of Deladumone at this stage did not alter the subsequent course of labor in any way. In 197 patients, the preparation did not induce any unwanted secondary effects (such as subsequent breast engorgement, change in the character of the lochia, or uterine bleeding), did not interfere with the postpartum physiological adjustments (involution of the uterus and resumption of normal cyclic ovarian activity) in any way, and did not induce bleeding or masculinization in any patient.

Comparative Efficacy of Deladumone Given Intramuscularly After Delivery or During Labor in Preventing Postpartum Lactation and Breast Engorgement, Review of 197 Cases

			Manifestations After Therapy					
			Completely Asymptomatic		Breast Pain		Breast Fulness	
Group	No. of Patients	Dose (Cc.) and Time of Administration	No.	%	No.	%	No.	%
1	51	2; within 1 to 2 hr. of delivery	22	43.1	15	29.4	22	43.1
2	49	3; during 3rd stage of labor	36	73.5	10	20.4	10	20.4
3	50	2; after 1st stage of labor	43	86.0	7	14.0	5	10.0
4	47	3; after 1st stage of labor	43	91.5	4	8.5	4	8.5

In group 1 (patients given 2 cc. of Deladumone immediately or within two hours after delivery) 22, or 43.1%, of the 51 patients were completely asymptomatic and comfortable during their hospitalization. In the others, some degree of pain and/or fulness developed, although the symptoms generally were mild to moderate and transitory in nature. Three patients responded favorably to a second dose of Deladumone. In four cases, application of ice packs was necessary to alleviate pain.

In group 2 (patients given 3 cc. of Deladumone during the third stage of labor), 36, or 73.5%, of the 49 patients showed an excellent response to the medication. Mild to moderate pain and/or fulness was observed in the remaining 13 women. One individual required the application of ice packs to relieve pain.

When Deladumone was given (in a dosage of 2 cc. as a single injection) between the first and second stages of labor, it completely prevented postpartum lactation and its sequelae in 43, or 86%, of the 50 patients in group 3. Some degree of pain, fulness, or both was experienced by the remaining seven women, and in two instances ice packs were applied. A second injection of the hormone preparation controlled the symptoms in two patients.

The patients in group 4 responded most favorably to treatment with Deladumone. Of 47 women (given a single 3-cc. injection between the first and second stages of labor), 43, or 91.5%, remained completely asymptomatic throughout the critical first five or six postpartum days. Only four women experienced a slight transitory fulness and tenderness of the breasts, and when discharged five days after delivery they also were asymptomatic. In view of the incomplete prevention of lactation and the unpredictable response which usually has characterized therapy with other hormonal agents, the results achieved in this group with Deladumone are considered to be excellent.

One patient in each of groups 1 and 2 decided to breast feed her infant after she had been treated with Deladumone. The suckling stimulus readily overcame the hormone-induced inhibition and lactation occurred without difficulty when the infant was placed to the breast. In the 197 women, no relationship could be established between the response to therapy and the age, the parity, or the previous nursing experience of the patients.

Comment

Hormone therapy offers a simple and effective means of achieving breast comfort in the new mother. The present study confirms the observation [5] that the time of administration is an important factor in determining the efficacy of the hormone treatment. At parturition, the emptying of the uterus activates the anterior pituitary gland to accelerate the production and release of the lactogenic hormone. Although in the past hormone therapy usually has been instituted as soon as possible after parturition and before suckling has taken place, many of the preparations used have been given by mouth, and consequently of necessity therapy has been delayed until the patient was able to tolerate oral medication. By the use of the long-acting hormone combination for parenteral administration, Deladumone, it has been possible in this investigation to initiate sustained hormonal inhibition of lactogenic hormone release during actual labor before the uterus has been emptied. The value of inducing inhibition of the pituitary gland before lactogenic hormone release is clearly demonstrated by the significantly greater number of patients who responded satisfactorily to the 3-cc. dose of Deladumone when the preparation was injected at the end of the first stage of labor than when it was given immediately or within two hours after delivery. In most instances, a single injection sufficed. Once the lactogenic hormone release is prevented by a sufficiently early administration of an adequate dose of Deladumone, the prolonged hormonal action of the preparation appears to supply sustained inhibition of lactation for a long enough time to permit the patient to make the necessary physiological readjustments to the elimination of breast feeding without experiencing the discomforts of undesirable breast manifestations. Finally, the balance of the hormonal components in Deladumone is such that it is possible to administer this preparation in a sufficiently large dose to prevent lactation without affecting the involution of the uterus, the character of the lochia, or the restoration of normal ovarian function.

Summary and Conclusions

The value of hormones in preventing lactation and engorgement of the breasts in the puerperium was investigated in 197 new mothers who were given a single injection of a balanced long-acting androgen-estrogen combination, Deladumone. In order to evaluate the influence of the time of administration and of the dosage on the effectiveness of Deladumone in controlling the breast manifestations, the patients were divided into four groups each of which was given a different regimen of treatment. The results indicated that the efficacy of the preparation depends particularly on the time of administration. Complete prevention of lactation and its sequelae was achieved in 91.5% of 47 patients by administering a single 3-cc. injection of Deladumone immediately after the end of the first stage of labor. Smaller amounts or equal doses given later in labor or after delivery were less effective. Deladumone was notably free from unwanted effects on the endometrium post partum, the involution of the uterus, and the subsequent ovarian function.

It is concluded that postpartum lactation and its associated breast manifestations can be predictably prevented in a very high percentage of non-nursing mothers by the administration of a single injection of at least 3 cc. of the long-acting hormone preparation Deladumone at the end of the first stage of labor.

270 Clinton Ave. (5) (Dr. Lo Presto).

The androgen-estrogen combination used in this study was supplied as Deladumone by E. R. Squibb & Sons, New York.

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IMPLICATIONS OF THE INCREASED INCIDENCE OF LEUKEMIA.—Perhaps it will eventually be recognized as one of the most significant medical features of the early twentieth century that, as a by-product of more and more powerful therapeutic procedures and the production of chemical substances outside biologic experiences, the normal protective barriers that kept mutagenic agents from the internal organs have been more and more frequently penetrated. Ionizing radiation is the most important, but the whole theme of this lecture is that other agents must be at work, with increasing leukemic incidence as the only evidence as yet of their presence. It may be only a tiny price that has to be paid for the advantages of a scientific civilization, but it is disquieting and it raises the lurking fear that anything that is increasing the incidence of leukemia may also be breaking through the other barriers that in the past have protected the germ cells from mutagens. I think one would be wise to pay more attention to leukemia even than its intrinsic interest and lethality demand, just because of the possibility that it is the best indicator one can have of the last and greatest danger to civilization, active and unavoidable genetic deterioration.—Sir Macfarlane Burnett, Leukemia as a Problem in Preventive Medicine, *The New England Journal of Medicine*, Aug. 28, 1958.

CLINICAL NOTES

CHORIOCARCINOMA

REPORT OF A CASE OF 25-YEAR SURVIVAL AFTER ORCHIECTOMY

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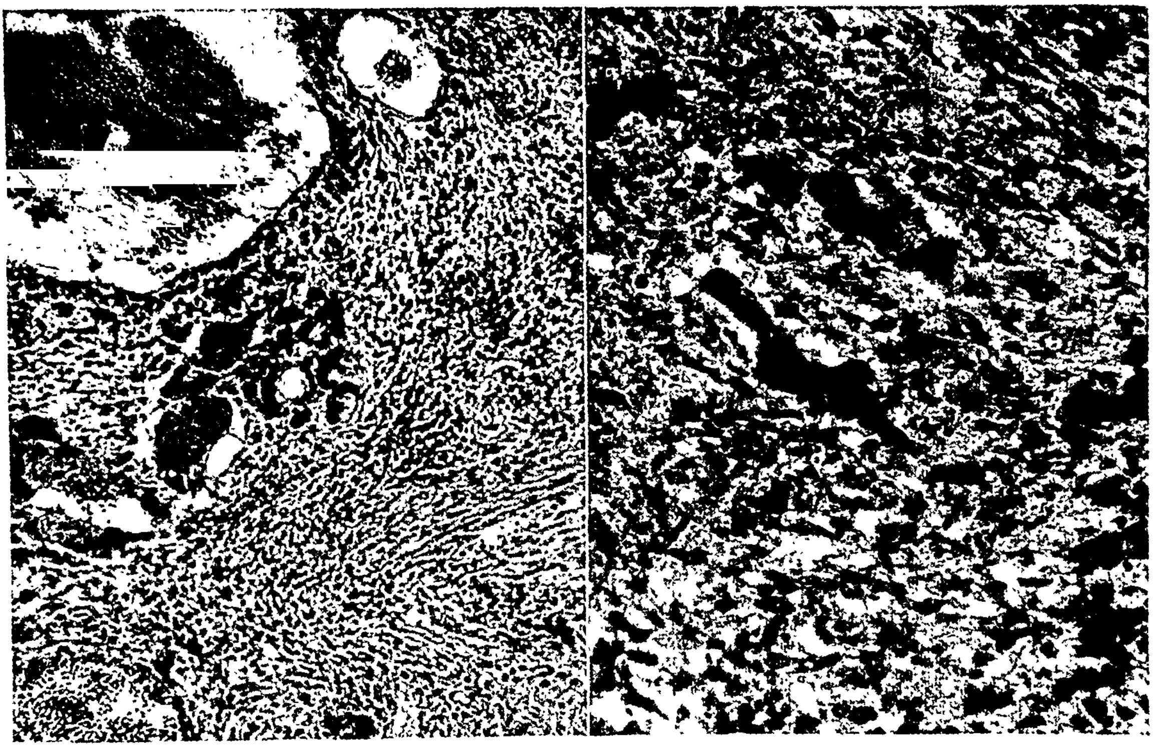
Choriocarcinoma (chorion epithelioma) is the most malignant tumor of the testis. It arises from teratoma or from cells capable of giving rise to teratoma. The presence of more mature teratoid differentiation in tumors containing choriocarcinoma is associated with reduction in malignancy displayed by the latter.[1] For certain definite periods, even the choriocarcinoma remains localized to the testis. Lewis[2] reported that 80% of patients with choriocarcinoma had metastases present at the time of admission to the hospital. In one-half of them the metastases caused the presenting symptoms. Of the 38 patients with choriocarcinoma reported by Lewis in 1949, one was alive six years after radical orchiectomy and prophylactic radiation therapy. This patient had no demonstrable metastases preoperatively, and teratoid tissue was found with the chorionic element. On reviewing the English literature we were unable to find a follow-up report on a patient with choriocarcinoma surviving as long as 25 years after diagnosis was made. It is the purpose of this paper to report such a case.



Left, choriocarcinoma. Cytotrophoblast is made up of characteristic uniform cells with clear cytoplasm. Syntrophoblast with dark eosinophilic cytoplasm is also seen. There is evidence of hemorrhage in large cystic areas. *Right,* high-power view of choriocarcinoma. Detail of cytotrophoblast and syntrophoblasts is evident.

A 25-year-old man was seen by his family physician on Aug. 1, 1933, for complaint of painless swelling of the right testis, which had been present for a few days. Attempted aspiration was unsuccessful at that time. His history was negative, except for orchitis of the left testis after mumps a few years previously. He was referred to the University Hospital for further diagnosis and treatment. He was seen in the outpatient clinic on Aug. 23, 1933. In the intervening three-week period the swelling had enlarged to the present size.

The general physical examination was essentially negative. The right scrotal sac was enlarged, and it appeared twice as large as the left. The enlargement involved the testis proper, which was smooth and stony hard; transillumination could not be done. The testis measured 4.5 cm. by 4 cm. There was diminished testicular sensation. The left testis was smaller than normal. Rectal examination revealed a normal prostate, and abdominal examination was unremarkable. Blood pressure was 124/68 mm. Hg. The routine ex-

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aminations, including blood and urine tests, were within normal limits. An Aschheim-Zondek (A-Z) test of a morning urine specimen showed a positive result of 3,300 mouse units. A chest film was reported negative. A tumor of right testis was suspected and hospitalization urged.

Orchiectomy on the right was performed on Aug. 29, 1933, with the patient under gas anesthesia. The usual scrotal incision was made, and high ligation of the spermatic cord was performed. After removal the testis was cut open and a 2.5-cm. soft and cellular tumor was found in the center. It was completely encapsulated and completely surrounded by normal testicular parenchyma. Within the tumor were several small necrotic masses.

Convalescence was uneventful, and the patient was discharged from the hospital on Sept. 2, 1933. Three weeks later on a follow-up study an A-Z test yielded less than 500 mouse units.

The microscopic sections (see figure) of the testicular tumor were described by Dr. C. V. Weller as follows: "Chorion epithelioma infiltrating testis. Neoplasm contains numerous syncitial cells. Areas of recent hemorrhage in neoplasm. Pressure atrophy of the testicular tubules. Vas and epididymis showed no pathology. Prognosis should be guarded." The late Dr. James Ewing of Cornell University reviewed the slides and confirmed the diagnosis in 1941.

Follow-up studies were done here regularly until 1938, and various physical examinations and urine tests were reported to be negative. After 1938 the follow-up has been through correspondence. The patient recently reported that he was in fine health and had celebrated his 49th birthday. In spite of his having had orchitis on the left due to mumps and orchiectomy on the right, he had two children after the operation and his sex life had been and is satisfactory.

With our recently renewed interest in this case, we reexamined the old slides and obtained new microscopic sections from the blocks of the tissue preserved since his operation, and Dr. M. Abell read them as follows: "Most of the tumor consists of chorion epithelioma but there are areas of teratocarcinoma seen in few sections."

Comment

Favorable prognostic signs in a case of testicular tumor are[1] (1) no pain, (2) negative urinary gonadotropins, (3) no metastases at the time of first examination, (4) no extension outside the testis, (5) no vascular invasion, and (6) no hyperplasia of interstitial cells. Size of the tumor and duration of symptoms have no significance as prognostic features. Of the patients who had positive urinary gonadotropins at the time of first examination, 69% were dead within two years. The patient described above had a positive A-Z test at 3,300 mouse units preoperatively, and results were negative a short time after orchiectomy. He did not have any pain, and no metastases were present at the time of first examination. No evidence of extension of the neoplasm outside the testis was noticed, nor was there any vascular invasion.

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ENTHESITIS—TRAUMATIC DISEASE OF INSERTIONS

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The human locomotor apparatus consists of an active motor system (muscles) and a passive system of transmission (bones and joints) connected by an intermediate formation, the muscular and tendinous insertions. The insertions must be differentiated from the other two systems both anatomically and functionally. These insertions are effected in three principal manners: (1) inlaid piercing into the bony substance through periosteum (tendinous insertion), (2) reinforcing fibrous bundles extending from tendon to ligaments, joint capsule, or other tendons (aponeurosis), and (3) direct adhesion to periosteum of the bone (muscular or tendinomuscular attachment).

The locations of these attachments are therefore spots where tissues of common mesenchymal origin, but often poorly differentiated, meet. Possibly for this reason, insertions show a peculiar reaction to irritative stimuli, often characterized by metaplastic phenomena. Most frequently these stimuli are of traumatic, particularly microtraumatic, origin. The continually recurring concentration of muscle stress at these points provokes a reaction of inflammation with a strong tendency to the formation of fibrosis and calcification. Enthesitis (Greek "enthesis" meaning insertion) is the name proposed to indicate this morbid event.

The sites of occurrence of this condition in the body are as various as the different repetitive muscular actions called for in different occupations as well as recreations. Those which are probably best known are to be found in the field of sports, such as (1) apophysitis of the cervical spine in wrestlers (La Cava), (2) enthesitis of teres major and minor, the "glass arm" of water-polo players and others who engage in hard throwing actions, (3) enthesitis of the medial epicondyle of the humerus, "tennis elbow," (4) enthesitis of the biceps in boxers, gymnasts, and baseball players, (5) enthesitis of the adductors in football (soccer) players, (6) "tibia rugosa" (La Cava), "shin splints" or tibial periostitis (Nitz and Presber) of sprinters, and (7) Achilles tendinitis in tennis players and skiers.

Differential Diagnosis

The clinical evolution of chronic enthesitis is naturally slow in the beginning and is not accompanied by the dramatic phenomena seen in cases

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Director of the Institute of Athletic Medicine.

of rupture of muscle or tendon. Slight pain in the area of the insertion, at first only toward the end of competition, or in carrying out exaggerated movements, is the first symptom. Finally, all movements of the affected muscle become painful. Often the patient is unable to localize the pain exactly and the diagnosis must then be made with the aid of functional tests to demonstrate abnormal or decreased muscle contraction and strength.

In the initial stage, the musculotendinous mass is felt to be of increased consistency, if the site is accessible to palpation. Tenderness is usually localized in the area of the insertion. Roentgenologic examination with use of soft tissue technique, will more or less regularly reveal calcification at the insertion, often extending for a considerable distance into the muscle.

Differentation from other chronic conditions involving the musculoskeletal, nervous, and connective tissues is ordinarily not difficult. In traumatic arthritis and periarthritis, all movements of the joint are painful, but in enthesitis only those are painful which bring into play the affected muscle. The pain of acute and chronic bursitis is usually more dull, constant, not entirely relieved by rest. Movement in bursitis may often produce a sort of whistle. Roentgenologic demonstration of calcification in a bursa may be conclusive. Subcutaneous fibrosis after bruising and hemorrhage and cellulitis may be difficult to distinguish if there is not a good history. In cronic neuritis, pain follows nerve pathways and tenderness is relative and not localized to the insertion.

Treatment

Effective management of this condition is hindered by the fact that the evolution of symptoms is so gradual that many athletes will not accept the necessary recommendation of total rest for the affected part until the condition is far advanced and can no longer be ignored. The results are naturally better, the earlier rest is started.

Rest may be integrated with certain forms of physiotherapy. Short wave treatment is particularly useful. The use of modulated currents according to Bernard's method may be helpful. The analgesic effect of these currents may allow the athlete with a mild case to continue some activity.

Injection of procaine in a long-acting form at the site of the pain is greatly favored by some writers on this subject. I am not convinced of its effectiveness except from the standpoint of pain relief. In fact, the evolution of certain injuries so treated suggests that the repeated introduction of this substance into the tissues, associated with the microtraumas of needle puncture, produces an aseptic inflammatory process in an already irritated region, which further aggravates the condition.

Roentgenotherapy is widely used as a radical method of treatment and to produce analgesia. Daily doses of 100 to 120 r in air are given for six to eight days. The results are often excellent. It must not be forgotten that this treatment, coupled with the natural disability due to the lesion, leaves a certain amount of muscular atrophy requiring an adequate period of retraining before complete function can be restored (Naves).

Surgical treatment is advisable in persistent cases which prove refractory to other methods. It is particularly indicated in cases where calcification has been demonstrated roentgenologically. The operation should be designed to remove the calcific formation and reestablish, if possible, the normal anatomic structure.

Foro Italico.

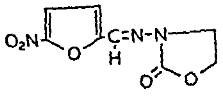
COUNCIL ON DRUGS

NEW AND NONOFFICIAL DRUGS

Monographs and supplemental statements on drugs described here and in subsequent editions of New and Nonofficial Drugs are based on the evaluation of available scientific data and reports of investigations.

H. D. Kautz, M.D., *Secretary.*

Furazolidone.—3-(5-Nitro-2-furfurylideneamino)-2-oxazolidinone.—The structural formula of furazolidone may be represented as follows:



Actions and Uses.—Furazolidone, a nitrofuran derivative, shows antibacterial activity in vitro against a variety of gram-negative and gram-positive enteric organisms, including species of Salmonella, Shigella, Escherichia, Proteus, Streptococcus, and Staphylococcus. It also shows antiprotozoal activity and has been incorporated in combination with other topical preparations for the treatment of trichomonal infections of the vagina. The precise mechanism of action of furazolidone is not fully understood, but the drug is believed to act by inhibiting dehydrogenase systems of the microbial cell.

Orally administered furazolidone is proposed for the treatment of bacterial diarrheal disorders and enteritis. Its usefulness for the foregoing purposes is based on subjective observations in a relatively small number of cases. Since many bacterial diarrheas are self-limited and of short duration, it is difficult to determine what part in the over-all clinical improvement of the patient might be ascribed to the action of the drug. Nevertheless, it is the clinical impression of observers that furazolidone is useful in the treatment of some patients with acute bacterial gastrointestinal upsets. The drug apparently is capable of arresting some infections due to strains of bacteria which are resistant to the usual antibiotics. Although well-controlled clinical studies are needed to establish its ultimate efficacy, furazolidone shows promise as a chemotherapeutic agent for bacterial enteritis and diarrhea.

In the clinical trials thus far, nausea and vomiting seem to be the most frequent side-effects to orally administered furazolidone. These symptoms usually subside upon reduction in dosage. In occasional patients, headache has been observed. A few patients have shown sensitization reactions in the form of a vesicular or morbilliform pruritic rash. This has disappeared upon cessation of treatment. Hypochromic anemia has been observed occasionally after long-term therapy, but it is not certain whether this effect is due to dietary factors rather than to the drug. Overgrowth of nonsusceptible organisms with resulting colitis, proctitis, anal pruritus, and monilial or staphylococcic enteritis has not been observed. There are no known absolute contraindications to the administration of furazolidone.

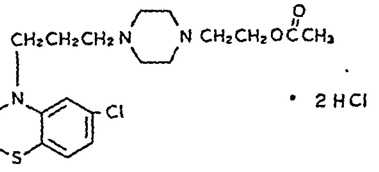
Dosage.—Furazolidone is administered orally. The usual dose for adults is 100 mg. four times daily. For children five years of age or older, the dose is 50 mg. four times a day. Dosage for children between 1 and 5 years of age is 25 to 33 mg. four times daily. For infants up to one year of age, 8 to 16 mg. is given four times a day. The maximum daily dose for adults and children should not exceed 7.5 mg. per kilogram of body weight, given in four divided doses over a period of 24 hours.

Preparations: suspension (oral) 3.33 mg. per cc.; tablets 100 mg.

Applicable commercial name: Furoxone.

Eaton Laboratories cooperated by furnishing scientific data to aid in the evaluation of furazolidone.

Thiopropazate Hydrochloride.—2-Chloro-10-{3-[4-(2-acetoxyethyl)piperazinyl]propyl}phenothiazine dihydrochloride.—The structural formula of thiopropazate hydrochloride may be represented as follows:



Actions and Uses.—Thiopropazate hydrochloride is a phenothiazine derivative with actions and uses similar to those of other agents of this type. Chemically and pharmacologically, it is most closely related to prochlorperazine and perphenazine. Thiopropazate is a potent compound, and it produces comparable pharmacological effects with doses that are considerably less than those of chlorpromazine. It has a spectrum of clinical usefulness akin to that of other phenothiazine derivatives and is subject to similar limitations. Available clinical evidence, although not well controlled, would indicate that the principal clinical application of thiopropazate will be in the management of psychoses in which agitation, tension, combativeness, and aggressiveness predominate. The drug is apparently capable of eliciting beneficial responses in some patients who fail to respond to other closely related compounds. It is also of value in some patients with psychomotor retardation, apathy, and lethargy. Animal experiments have shown that the drug possesses potent antiemetic properties, but it has not been evaluated clinically for this purpose.

Certain typical phenothiazine side-effects such as sedation and hypotension have been reported to be less frequent and less severe with thiopropazate than with other agents of this class, particularly chlorpromazine. Although the drug has produced leukopenia, no cases of granulocytopenia have been recorded to date. Likewise, jaundice has not occurred during its clinical trial. In view of the phenothiazine structure of thiopropazate, however such untoward reactions should be watched for The most frequent and troublesome side-effect of this drug has been Parkinson-like symptoms referable to extrapyramidal involvement. Tremors, rigidity, fixed facies, and drooling frequently complicate therapy with this agent. Although such neurological effects appear to be a function of dosage, there is a very narrow range between clinically effective doses and those causing extrapyramidal symptoms

The usual contraindications to phenothiazine derivatives in general apply to thiopropazate and include patients with severe depressions, those with liver damage, and persons under the influence of other central nervous system depressants. The drug should not be given to patients with convulsive disorders.

Dosage.—Thiopropazate hydrochloride is administered orally in doses which must be individualized according to the severity of the condition under treatment, the response of the particular patient, and the appearance of side-effects.

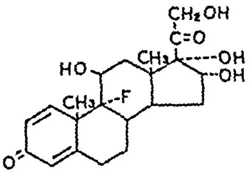
For the management of patients with psychotic conditions, the usual initial dose is 10 mg. three times a day. This dose is then adjusted upward or downward in daily increments of 10 mg. given at intervals of three or four days, according to therapeutic response. At present, 100 mg. per day should be considered a maximum dose. For anxiety tension states, psychosomatic conditions, and other neuroses, the foregoing dosage schedule is reduced by half.

Preparations: tablets 5 mg. and 10 mg.

Applicable commercial name: Dartal Dihydrochloride.

G. D. Searle & Co. cooperated by furnishing scientific data to aid in the evaluation of thiopropazate hydrochloride.

Triamcinolone.—9α-Fluoro-16α-hydroxyprednisolone.—The structural formula of triamcinolone may be represented as follows:



Actions and Uses.—Triamcinolone is a potent glucocorticoid with anti-inflammatory, hormonal, and metabolic effects similar to those of prednisolone. It has an anti-inflammatory potency greater than that of an equal amount of prednisolone; i. e., comparable suppressive effects may usually be achieved with lower doses of triamcinolone than with prednisolone. Triamcinolone lacks the sodium-retaining and edema-producing effects of most other glucocorticoids. During the first several days of administration, it may cause a loss of sodium from the body; an initial mild diuretic action is frequently observed, whether the patient is frankly edematous or not. This is in contrast to the definite sodium-retaining and fluid-retaining properties of cortisone and hydrocortisone and to a much lesser extent with prednisone and prednisolone. Except in exceedingly large doses, triamcinolone apparently has no consistent effect on potassium excretion. Hence, neither sodium restriction nor potassium supplementation is ordinarily required during therapy with this agent. As with other glucocorticoids, the long-term administration of triamcinolone results in definite catabolic effects, as indicated by impairment of carbohydrate utilization and negative protein and calcium balance. This catabolic effect, coupled with a lack of appetite stimulation which is apparently peculiar to triamcinolone, may produce weight loss that might be undesirable in some patients treated for long periods of time. However, the voracious appetite, with weight gain and euphoria, characteristic of other steroids, is not seen with administration of triamcinolone.

Triamcinolone has been used for the management of a wide variety of clinical conditions usually considered amenable to systemic steroid therapy. These have included rheumatoid arthritis and other collagen diseases, allergic and dermatological disorders, certain leukemias and malignant lymphomas, the nephrotic syndrome, pulmonary emphysema and fibrosis, acute bursitis, rheumatic fever, and certain blood dyscrasias. Although clinical experience with the drug in some of the foregoing conditions is not extensive, the many similarities in action between triamcinolone and other potent glucocorticoids would indicate a usefulness for triamcinolone akin to that of other agents of this class. There is some evidence that triamcinolone is more effective at a smaller dosage than are other steroids in controlling both the skin and the joint lesions in psoriasis, whether or not complicated by arthropathy. Because it does not exert strong mineralocorticoid effects, triamcinolone is probably not as effective as cortisone or hydrocortisone for the management of acute adrenal insufficiency. Triamcinolone appears to compare favorably with other steroids for use in those situations in which edema and sodium retention have been complicating problems. It may also be the steroid of choice for patients in whom psychic stimulation, euphoria, voracious appetite, and weight gain should be avoided. Like all other hormones of this type, triamcinolone suppresses, but does not cure, the manifestations of the various diseases treated.

Although electrolyte imbalance rarely complicates therapy with triamcinolone, the drug does produce the other side-effects and untoward reactions common to the glucocorticoids. At therapeutically equivalent doses, the frequency and severity of clinical manifestations of hyperadrenalism—rounding of the face, fat deposition, and hirsutism—are essentially the same. Likewise, there is little indication that the relative incidence of osteoporosis is materially decreased after the long-term use of the drug. Triamcinolone apparently does not cause the euphoria sometimes seen with other steroids, and the occurrence of mental depressions is uncommon. Current evidence suggests that the drug may not produce as high an incidence of peptic ulcer as do other steroids. Cutaneous erythema seems to be a side-effect peculiar to triamcinolone. The usual contraindications and precautions of glucocorticoid therapy should be followed in the use of triamcinolone, keeping in mind that prolonged therapy with this drug will suppress the function of the patient's own adrenals by interfering with the pituitary-adrenal axis.

Dosage.—Triamcinolone is administered orally. Dosage varies with the condition being treated, its severity, appearance of side-effects, and individual response. For the common diseases amenable to systemic steroid therapy, the usual initial (suppressive) dose for adults ranges from 8 to 20 mg. per day in three or four divided doses. When a satisfactory response is obtained, the initial dose is reduced gradually in decrements of 2 mg. every two or three days until a maintenance dosage level is reached which will adequately maintain the patient's condition. For the treatment of rheumatoid arthritis, the necessity of large initial doses, with subsequent step-wise reduction to maintenance levels, has been questioned by some authorities who favor, instead, the initiation of therapy with doses believed to be the eventual maintenance dose.

Preparations: tablets 1.2 mg. and 4 mg.

Applicable commercial name: Aristocort, Kenacort.

Lederle Laboratories Division, American Cyanamid Company, cooperated by furnishing scientific data to aid in the evaluation of triamcinolone.

THE JOURNAL
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DIABETES AND PREGNANCY

THE management of the diabetic-obstetric patient is an individual matter with each woman. The pregnant diabetic woman should be examined frequently, especially in the latter half of the pregnancy. She should then be seen once a week and, at times, twice a week. During pregnancy a normal blood sugar level should be maintained with the use of as much insulin as necessary. Diabetes frequently becomes more severe in the sixth or seventh month of pregnancy, and the patient may require more insulin during this period. A diet for a diabetic-obstetric patient should be given, averaging 30 calories per kilogram of increasing body weight and containing 175 to 250 Gm. of carbohydrate, 2 Gm. of protein per kilogram of body weight, and a sufficient amount of fat to complete the diet. For example, a patient weighing 132 lb. (60 kg.) would require 1,800 calories initially. An attempt should be made to limit the weight gain to about 15 lb. (6.8 kg.). The diet should be low in salt to prevent edema as well as toxemia of pregnancy. In some cases ammonium chloride is also given to prevent edema, but, since ammonium chloride has an acidotic property, the dosage must be watched carefully, with daily urine tests for acetone. When edema or hydramnios is present, meralluride sodium in 1-to-2-cc. doses may be given intramuscularly at weekly intervals if no renal damage is present.

The early timing of delivery in such patients is important. The patient with an uncomplicated case should be delivered by about the end of the 37th week of pregnancy. It is usually in the last three weeks of pregnancy that most intrauterine deaths occur in patients with diabetes. Diabetic women with obvious vascular damage are delivered at the end of the 35th week. Potentially diabetic persons who require no insulin but have an abnormal sugar tolerance are allowed to go to term and are treated as nondiabetic patients. Early induction of labor or cesarean section with the patient under spinal anesthesia is indicated. While patients may be delivered through the pelvis, if the baby is not large and if the pelvis is adequate, infants of diabetic mothers do not often survive pelvic trauma. In some series of cases, as many as 70% of pregnant diabetic women have been delivered by cesarean operation, and this includes patients with repeat cesarean sections. If a patient is taking long-acting insulin, it should be withdrawn for 24 hours before the delivery or operation. Regular insulin is substituted, and one-third of the total daily dose is given before each meal. During prolonged labor or during surgery, regular insulin in dextrose should be given intravenously, about 25% of the total daily dose of insulin per 50 Gm. of dextrose. It must be remembered that the immediate care of the newborn premature baby is most important, particularly in preventing hyaline membrane disease. A physician should be present whose only duty is to take proper care of the infant at once.

The value of female sex hormone therapy has been a controversial subject, and the matter is not yet settled. White and associates[1] believe that the parenteral administration of female sex hormones gives added protection to the mother and the fetus when pregnancy complicates diabetes and especially in those patients with vascular damage. In contrast, others disagree completely.

The Medical Research Council of Great Britain[2] appointed a committee to conduct a controlled clinical trial to assess the effect, if any, of oral administration of female sex hormones on fetal survival rate in pregnant diabetic women. These studies took place in nine hospital centers where two comparable groups were observed, with and without therapy with female sex hormones. The frequency of stillbirths and neonatal deaths in the two groups proved to be almost the same. However, in this study, the hormones were given orally and patients with cardiovascular complications were excluded. White, on the other hand, gave the hormones parenterally and included patients with cardiovascular complications. Blotner, at the Beth Israel Hospital in Boston, as a rule does not give hormone therapy. Favorable results have been obtained with proper care of the diabetic patient and early timing of delivery.

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1. White, P.; Gillespie, L.; and Sexton, L.: Use of Female Sex Hormone Therapy in Pregnant Diabetic Patients, Am. J. Obst. & Gynec. **71**:57-69 (Jan.) 1956.

2. Use of Hormones in Management of Pregnancy in Diabetics, Report to Medical Research Council by Their Conference on Diabetes and Pregnancy, Lancet **2**:833-836 (Oct. 22) 1955.

Optimum diabetic therapy and prenatal care, along with optimum obstetric judgment and management, are of prime importance in the care of a pregnant diabetic patient.

REPORT OF COMMISSION ON MEDICAL CARE PLANS

Accompanying this issue of The Journal is a 96-page Special Edition which contains the Findings, Conclusions, and Recommendations of the Commission on Medical Care Plans appointed by the Board of Trustees of the A. M. A. in November, 1954. This report on the types of medical care plans in existence throughout the United States deals with three broad areas of research: (1) the nature and method of operation of the various types of plans through which persons receive the services of physicians, (2) the effect of these plans on the quality and quantity of medical care, and (3) the legal and ethical status of the arrangements used by these plans. In the preface, Dr. Leonard W. Larson, Chairman of the Commission, states: "The Commission's study has attempted to summarize and correlate the various points of views, attitudes, and opinions of groups directly concerned in the provision of medical care. It presents information which has not been made available heretofore. It recommends possible solutions to perplexing problems. It also raises questions which have yet to be answered."

In this report is the product of three and one-half years of research on issues which involve every physician as an individual and the profession as a whole. It deserves study and discussion by all physicians before it is considered by the House of Delegates of the American Medical Association in Atlantic City in June, 1959. Although it was presented at the Clinical Session in Minneapolis in December, 1958, no definitive action was taken, pending further study by the constituent medical associations.

COUNCIL ON MEDICAL EDUCATION AND HOSPITALS

FIFTY-FIFTH ANNUAL CONGRESS ON MEDICAL EDUCATION AND LICENSURE

Palmer House, Chicago
Feb. 7-10, 1959

Sponsors: Council on Medical Education and Hospitals of the American Medical Association
Advisory Board for Medical Specialties
Federation of State Medical Boards of the United States

The 55th Annual Congress on Medical Education and Licensure, co-sponsored by the Council on Medical Education and Hospitals of the American Medical Association, the Advisory Board for Medical Specialties, and the Federation of State Medical Boards of the United States will be held Feb. 7-10, 1959, at the Palmer House in Chicago. The Federation will hold its Third Examination Institute on Feb. 7 and on Feb. 10 will consider curriculum changes and their implications to licensure. During Feb. 8 and 9 the Council and the Advisory Board will center attention on "Specialism and Research" as crucial factors in modern medical education and training.

The workshop-conferences scheduled for Sunday afternoon, Feb. 8, are being developed around panels of 15 to 20 selected participants. These panel conferences will be conducted in rooms which will each accommodate up to approximately 300 individuals who might desire to attend and participate in any of the four areas under consideration.

The co-sponsors are pleased to present the following program which has been planned for the 55th Annual Congress on Medical Education and Licensure.

Saturday, Feb. 7, 8:30 a.m. to 4 p.m.

Federation of State Medical Boards of the United States—Third Examination Institute

8:30 a.m. Plenary Session—Room 14
Stiles D. Ezell, M.D., Moderator
Secretary, New York Board of Medical Examiners
Opening Remarks
Introduction

10:00 a.m. Physiology—Room 17
Harold G. Wiggers, Ph.D., Dean, Albany Medical College of Union University
Preventive Medicine—Room 18
H. W. Brown, M.D., Professor of Parasitology, Columbia University College of Physicians and Surgeons

2:00 p.m. Biochemistry—Room 17
Phillip Cohen, M.D., Professor of Physiological Chemistry, University of Wisconsin Medical School
Internal Medicine—Room 18
James A. Campbell, M.D., Professor of Medicine, University of Illinois, College of Medicine

Advisory Board for Medical Specialties

9:00 a.m. Business Meeting—Crystal Room

Sunday, Feb. 8

2:00 p.m. Annual Meeting—Room 14
Roll Call
Report of Secretary-Treasurer
Appointment of Committees
Reports:
- Examination Institutes of 1958
- Public Relations
- Educational Council for Foreign Medical Graduates, Inc.
- Legislative Advisory Committee
- Constitution and Bylaws

8:00 p.m. Conference of Secretaries of State Medical Boards—Room 14

Sunday, Feb. 8

Council on Medical Education and Hospitals, American Medical Association
Advisory Board for Medical Specialties
Specialism in Medicine
First Plenary Session—Ball Room

Nothing out of its place is good and nothing in its place is bad.—Walt Whitman

Leland S. McKittrick, M.D., Presiding

9:00 a.m. Address of Welcome
Gunnar Gundersen, M.D., President, American Medical Association

9:10 a.m. Why This Conference?
Leland S. McKittrick, M.D., Chairman, Council on Medical Education and Hospitals, American Medical Association
Ernest L. Stebbins, M.D., President, Advisory Board for Medical Specialties

9:20 a.m. The Rise of Specialism in Modern Society
Paul M. Gross, Ph.D., Vice-president, Duke University

9:50 a.m. Specialism and the Pursuit of Excellence
Moody E. Prior, Ph.D., Dean, Northwestern University Graduate School

10:20 a.m. Specialism in Medicine Today and Tomorrow's Trends
Iago Galdston, M.D., Secretary, Committee on Medical Information, New York Academy of Medicine

10:50 a.m. Intermission

11:00 a.m. Challenges and Objectives of Specialism in Graduate Education for the Basic Medical Sciences
S. Marsh Tenney, M.D., Director of Medical Sciences, Dartmouth Medical School

11:30 a.m. Challenges and Objectives of Specialism in Graduate Education for the Clinical Sciences
Herman E. Pearse, M.D., Professor of Surgery, University of Rochester School of Medicine and Dentistry

12:00 noon Maintenance of Standards in Graduate Medical Education
Edward L. Turner, M.D., Secretary, Council on Medical Education and Hospitals, American Medical Association

2:00-5:00 Workshop-Conferences

After the initial plenary session there will be a series of *open* workshop-conferences focused on "Specialism in Medicine" from the standpoint of (*a*) the Residency Program, (*b*) the Specialty Board, (*c*) the Resident and Fellow, and (*d*) the Hospital. In each of these discussion groups there will be an invited panel of 15 to 20 distnguished participants. Others attending the Congress will have the opportunity to join the group of their own choice, insofar as possible. The conclusions, summaries, and recommendations of each of these conferences will be presented for general discussion at the Plenary Session on the afternoon of Feb. 9. Location of workshops will be announced.

Monday, Feb. 9

Council on Medical Education and Hospitals, American Medical Association
The Role of Research in the Education of All Physicians
Second Plenary Session—Ball Room

The origin of all science is in the desire to know causes; and the origin of all false science and imposture is in the desire to accept false causes rather than none; or, which is the same thing, in the unwillingness to acknowledge our own ignorance.—William Hazlitt

James M. Faulkner, M.D., Presiding

9:00 a.m. Research and Training
Conrad A. Elvehjem, Ph.D., President, University of Wisconsin

9:40 a.m. The Contribution of Research Orientation and Methods to the Educational Objectives of the Basic Medical Sciences
Wm. H. Hubbard Jr., M.D., Associate Dean, New York University College of Medicine

10:00 a.m. The Contribution of Research Orientation and Methods to the Educational Objectives of the Clinical Sciences
Nathan A. Womack, M.D., Professor of Surgery, University of North Carolina School of Medicine

10:20 a.m. The Role of Research in Graduate Medical Education
James A. Campbell, M.D., Professor of Medicine, University of Illinois College of Medicine

10:40 a.m. Intermission

11:00 a.m. The Research Orientation and the Teacher of Medicine
Isidore Snapper, M.D., Director of Medicine and Medical Education, Beth-El Hospital, Brooklyn

11:20 a.m. The Research Orientation and the Practitioner of Medicine
Warde B. Allan, M.D., Associate Professor of Medicine, Johns Hopkins University School of Medicine; Member, Council on Medical Education and Hospitals, American Medical Association

11:40 a.m. Maintenance of the Synergistic Relationship of Education and Research in Medicine
James A. Shannon, M.D., Director, National Institutes of Health

12:00 noon Open Discussion

Monday, Feb. 9

Council on Medical Education and Hospitals, American Medical Association
Advisory Board for Medical Specialties
Specialism in Medicine
Third Plenary Session—Ball Room
Leland S. McKittrick, M.D., Presiding

2:00 p.m. The Role of Medical Education in Civil and Defense Mobilization
John S. Patterson, Deputy Director, Office of Civil and Defense Mobilization

2:30 p.m. Report of Workshop-Conference Groups on Specialism in Medicine
(*a*) The Residency Program
Wright Adams, M.D., Chairman
George A. Wolf Jr., M.D., Rapporteur
(*b*) The Specialty Board
John McK. Mitchell, M.D., Chairman
Sam W. Banks, M.D., Rapporteur

(*c*) The Resident and Fellow
A. McGehee Harvey, M.D., Chairman
George G. Reader, M.D., Rapporteur
(*d*) The Hospital
Joseph C. Hinsey, Ph.D., Chairman
John Conlin, M.D., Rapporteur
Open Discussion

Monday, Feb. 9

Federation of State Medical Boards of the United States
Annual Federation Dinner and Walter L. Bierring Lecture—Crystal Room
6:30 p.m. Dinner
8:00 p.m. The Fourth Annual Walter L. Bierring Lecture
Gunnar Gundersen, M.D., President American Medical Association

Tuesday, Feb. 10

Program of Federation of State Medical Boards
Wesley D. Richards, M.D., Presiding
9:00 a.m. Red Lacquer Room
A Blending of Interests—Presidential Address
Wesley D. Richards, M.D., President, Federation of State Medical Boards of the United States; President, Pennsylvania State Board of Medical Education and Licensure
9:30 a.m. Major Changes in the Medical Curriculum During the Past Fifty Years
Willard C. Rappleye, M.D., President, Josiah Macy Jr. Foundation
10:00 a.m. Some Major Factors Involved in Reconstructing the Medical Curriculum
(*a*) Integration of Arts and Sciences with Medicine
Thomas B. Turner, M.D., Dean
Johns Hopkins University School of Medicine
(*b*) The Social Sciences in Medical Education
Milton Terris, M.D., Professor of Epidemiology, Tulane University School of Medicine
(*c*) Research as a Teaching Tool
S. Marsh Tenney, M.D., Director of Medical Sciences, Dartmouth Medical School
(*d*) The Future Position of the Internship—A medical school or a postgraduate responsibility which may lead to more radical changes
James A. Campbell, M.D., Professor of Medicine, University of Illinois College of Medicine
(*e*) Factors of Future Significance Which May Lead to Further Changes
John A. D. Cooper, M.D., Assistant Dean, Northwestern University Medical School
12:30 p.m. Luncheon and Annual Business Meeting—Crystal Room

WORKSHOP-CONFERENCE PARTICIPANTS

The Residency Program

Wright Adams, M.D., *Chairman*, Professor and Chairman, Department of Medicine, University of Chicago School of Medicine

George A. Wolf Jr., M.D., *Rapporteur*, Dean, University of Vermont College of Medicine

Warde B. Allan, M.D., Associate Professor of Medicine, Johns Hopkins University School of Medicine; Member, Council on Medical Education and Hospitals, American Medical Association

James Z. Appel, M.D., Member, Board of Trustees, American Medical Association

Walter Lyon Bloom, M.D., Director of Medical Education and Research, Piedmont Hospital, Atlanta

Thomas H. Brem, M.D., Professor of Medicine, University of Southern California School of Medicine

Robin C. Buerki, M.D., Executive Director, Henry Ford Hospital, Detroit

Louis A. Buie, M.D., Secretary-Treasurer, Advisory Board for Medical Specialties

John W. Cline, M.D., Associate Clinical Professor of Surgery, Stanford University School of Medicine; Member, Council on Medical Education and Hospitals, American Medical Association

John E. Deitrick, M.D., Dean, Cornell University Medical College

Stiles D. Ezell, M.D., Secretary, New York Board of Medical Examiners; Associate Secretary, Federation of State Boards of the United States

Theresa Falaguerra, Assistant Project Director, Bureau of Applied Social Research, Columbia University

Perrin H. Long, M.D., Chairman, Department of Medicine, State University of New York Downstate Medical Center

Cleon A. Nafe, M.D., Associate Professor of Surgery, Indiana University School of Medicine; Member, Board of Trustees, American Medical Association

John Parks, M.D., Dean, George Washington University School of Medicine

Malcom E. Phelps, M.D., American Academy of General Practice

S. Marsh Tenney, M.D., Director of Medical Sciences, Dartmouth Medical School

Nathan A. Womack, M.D., Professor of Surgery, University of North Carolina School of Medicine

The Specialty Board

John McK. Mitchell, M.D., *Chairman*, Dean, University of Pennsylvania School of Medicine

Sam W. Banks, M.D., *Rapporteur*, Secretary-Treasurer, American Board of Orthopaedic Surgery

Orpheus J. Bizzozero, M.D., Director of Medical Education, Waterbury Hospital, Connecticut

Hugh R. Butt, M.D., Department of Medicine, Mayo Clinic

James M. Faulkner, M.D., Medical Director, Homberg Memorial Infirmary, Massachusetts Institute of Technology; Member, Council on Medical Education and Hospitals, American Medical Association

George M. Fister, M.D., Clinical Lecturer in Surgery, University of Utah College of Medicine; Member, Board of Trustees, American Medical Association

Iago Galdston, M.D., Secretary, Committee on Medical Information, New York Academy of Medicine

Walter G. Maddock, M.D., Professor of Surgery, Northwestern University Medical School

Emily Mumford, Research Assistant, Bureau of Applied Social Research, Columbia University

Francis J. Nash, M.D., Kansas State Board of Medical Examiners

Herman E. Pearse, M.D., Professor of Surgery, University of Rochester School of Medicine and Dentistry

Paul S. Rhoads, M.D., Professor of Medicine, Northwestern University Medical School

Jesse D. Rising, M.D., Associate Professor of Medicine and Pharmacology, University of Kansas School of Medicine

Rufus B. Robins, M.D., Member, Board of Trustees, American Medical Association

Charles T. Stone, M.D., Professor of Internal Medicine, University of Texas Medical Branch; Member, Council on Medical Education and Hospitals, American Medical Association

Thomas B. Turner, M.D., Dean of the Medical Faculty, Johns Hopkins University School of Medicine

David B. Wilson, M.D., Director, University Hospital, University of Mississippi Medical Center

The Resident and Fellow

A. McGehee Harvey, M.D., *Chairman*, Professor of Medicine and Director of the Department of Medicine, Johns Hopkins University School of Medicine

George G. Reader, M.D., *Rapporteur*, Professor of Medicine, Cornell University Medical College

W. Linwood Ball, M.D., Vice-president, American Medical Association; Member, Board of Trustees, American Medical Association

John Z. Bowers, M.D., Dean, University of Wisconsin School of Medicine; Member, Council on Medical Education and Hospitals, American Medical Association

David A. Boyd Jr., M.D., Secretary-Treasurer, American Board of Psychiatry and Neurology

W. Andrew Bunten, M.D., Member, Council on Medical Education and Hospitals, American Medical Association

Guy A. Caldwell, M.D., Department of Orthopedics, Ochsner Clinic; Member, Council on Medical Education and Hospitals, American Medical Association

John S. DeTar, M.D., American Academy of General Practice

Robert J. Glaser, M.D., Dean, University of Colorado School of Medicine

William N. Hubbard Jr., M.D., Associate Dean, New York University College of Medicine

Hugh H. Hussey, M.D., Dean, Georgetown University School of Medicine; Member, Board of Trustees, American Medical Association

Patricia Kendall, Project Director, Bureau of Applied Social Research, Columbia University

L. W. Larson, M.D., Chairman, Board of Trustees, American Medical Association

Russell A. Nelson, M.D., Director, Johns Hopkins Hospital

Isidore Snapper, M.D., Director of Medicine and Medical Education, Beth-El Hospital, Brooklyn

Ernest L. Stebbins, M.D., Dean, Johns Hopkins University School of Hygiene and Public Health; President, Advisory Board for Medical Specialties

Henry S. M. Uhl, M.D., Director of Medical Education and Research, Springfield Hospital, Massachusetts

The Hospital

Joseph C. Hinsey, Ph.D., *Chairman*, Director, the New York Hospital-Cornell Medical Center

Richard Christie, Ph.D., Adjunct Professor of Psychology, Columbia University

John Conlin, M.D., *Rapporteur*, Medical Director, Boston City Hospital

W. Reece Berryhill, M.D., Dean, University of North Carolina School of Medicine

James A. Campbell, M.D., Professor of Medicine, University of Illinois College of Medicine

Harlan English, M.D., Member, Council on Medical Education and Hospitals, American Medical Association

Rev. John J. Flanagan, S.J., Executive Director, the Catholic Hospital Association of the United States and Canada

Holland T. Jackson, M.D., President, American Academy of General Practice

Victor Johnson, M.D., Director, Mayo Foundation for Medical Education and Research

Edwin H. Lawson, M.D., President-elect, Federation of State Medical Boards of the United States

Herbert E. Longnecker, Ph.D., Vice-president, Chicago Professional Colleges, University of Illinois

Robert I. McClaughry, M.D., Professional Associate, Division of Medical Sciences, National Academy of Sciences, National Research Council

Raymond M. McKeown, M.D., Member, Board of Trustees, American Medical Association

Julian P. Price, M.D., Member, Board of Trustees, American Medical Association

Willard C. Rappleye, M.D., President, Josiah Macy Jr. Foundation

James A. Shannon, M.D., Director, National Institutes of Health

George W. Stephenson, M.D., Assistant Director, American College of Surgeons

W. Clarke Wescoe, M.D., Dean of the School of Medicine and Director of the Medical Center, Professor of Pharmacology and Experimental Medicine, University of Kansas; Member, Council on Medical Education and Hospitals, American Medical Association

Participants-at-Large

Leland S. McKittrick, M.D., Chairman, Council on Medical Education and Hospitals, American Medical Association

Ray Amberg, Ph.D., President, American Hospital Association

F. J. L. Blasingame, M.D., Executive Vice-president, American Medical Association

Edwin L. Crosby, M.D., Director, American Hospital Association

Ward Darley, M.D., Executive Director, Association of American Medical Colleges

Conrad A. Elvehjem, Ph.D., President, University of Wisconsin

Lester J. Evans, M.D., Executive Associate, The Commonwealth Fund

Paul M. Gross, Ph.D., Vice-president, Duke University

Gunnar Gundersen, M.D., President, American Medical Association

Ernest B. Howard, M.D., Assistant Executive Vice-president, American Medical Association

Louis M. Orr, M.D., Preident-elect, American Medical Association

Moody E. Prior, Ph.D., Dean, Northwestern University

MEDICAL NEWS

ARKANSAS

Dr. Fitch Wins Vitamin Award.—Dr. Coy D. Fitch Jr., an intern at the University of Arkansas Medical Center, Little Rock, has won the three-year Russell M. Wilder Fellowship of the National Vitamin Foundation, given to one man in the nation each year and made to "medical scientists who show great promise in research on nutrition and metabolism problems." Dr. Fitch, a native of Beebe, was awarded the Faculty Key as "the graduating student whose scholastic abilities, personality, and character best qualified him to become a physician" when he graduated from the University of Arkansas School of Medicine last June. Under the terms of the fellowship, the foundation will give the university $16,500 over the next three years to support Dr. Fitch's work toward a doctor of philosophy degree in biochemistry, to complete his residency in medicine, and to carry out research projects.

CALIFORNIA

Obstetrical and Gynecological Assembly.—The 14th annual Mid-Winter Meeting of the Obstetrical and Gynecological Assembly of Southern California will be held at The Ambassador Hotel, Los Angeles, Feb. 9-13. Registration to the assembly is limited to those certified by the American Board of Obstetrics and Gynecology; to those who have shown continuing interest in the meetings; and to members of the Los Angeles Society. The faculty will include Dr. Allan C. Barnes, Western Reserve University School of Medicine, Cleveland; Dr. Ronald R. Greene, Northwestern University Medical School, Chicago; Dr. Milton L. McCall, Louisiana State University Unit, Charity Hospital, New Orleans; Dr. Clyde L. Randall, University of Buffalo; and Dr. S. R. M. Reynolds, Ph.D., University of Illinois College of Medicine, Chicago. The assembly will include lectures, exhibits, and luncheon and round-table conferences. The lectures and discussions of this assembly will not be available in printed form. For information, write The Committee, P. O. Box 57118, Flint Station, Los Angeles 57.

ILLINOIS

Foreign Speaker.—Modern Concepts in Psychiatry, seminar series held at Veterans Administration Hospital, Downey, Oct. 20, featured "The Deprivation Experiment (Its Limitations and Its Value as a Means to Separate Learned and Unlearned Elements of Behaviour)" by Dr. Konrad Lorenz, Max Planck Institute for Comparative Ethology, Seewiesen, Oberbayern, Germany.

Chicago

Unit to Aid Science Exhibitors.—The Sigma Xi Club at Chicago Medical School provides counseling and help to such persons at Chicago and surban high schools who may be preparing exhibits or demonstrations for science fairs on ways to make exhibits more dramatic or functionally useful through animation and the introduction of live material. The club is now expanding this program to area high schools with the establishment of a speakers bureau. Members of the faculty will be made available as speakers to high school science clubs. Officers of the Sigma Xi Club at Chicago Medical School are: Leo J. Saidel, Ph.D., president; John L. Nickerson, Ph.D., vice-president; Dr. Emanuel Marcus, secretary; Jay A. Smith, Ph.D., treasurer.

University News.—Dr. Arvid Carlsson, associate professor of pharmacology at the University of Lund, Sweden, spoke on "Pharmacology of the Catecholamines" at a seminar at Chicago Medical School Oct. 27. Dr. Carlsson's talk was sponsored by the Sigma Xi Club at the school, which acted as his host for the West Side Medical Center.——The Chicago Medical School has announced an expansion of its current Residency Training Program in Psychiatry and Neurology under a newly established grant of $15,500 from the U. S. Public Health Service. The program is approved for three years and will use the facilities of Mount Sinai Hospital, the Illinois State Psychiatric Institute, and the West Side V. A. Neuropsychiatric Hospital and clinics. Dr. Harry H. Garner, chairman, department of psychiatry and neurology, is director of the program.

Plan Diagnostic Center.—Plans for construction of a Diagnostic Center Building for the University of Chicago Clinics have been announced by Maurice Goldblatt, chairman of the University of Chicago Cancer Research Foundation, who disclosed that ground for the new center probably will be broken in January. The two-story building will be built across Drexel Avenue near 59th Street on the University of Chicago campus. It will "link" Chicago Lying-in Hospital and Billings Hospital, both of which are part of the University of Chicago Clinics. Total construction cost of the new Diagnostic Cen-

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Physicians are invited to send to this department items of news of general interest, for example, those relating to society activities, new hospitals, education, and public health. Programs should be received at least three weeks before the date of meeting.

ter Building will be $1,300,000, with $850,000 for the building itself and $450,000 for structural alterations in adjacent buildings. The top floor of the structure will house clinical laboratories and chest and stomach x-ray microfilming apparatus for routine disease detection. The basement will serve as a corridor for transferring patients between Chicago Lying-in Hospital and the rest of the medical center. The sub-basement will house facilities for maintaining and storing medical records.

KENTUCKY

Dr. Lacovara Awarded Trophy.—At the seventh annual Attorney General's Training Series of the U. S. Department of Justice held at the Border Patrol Academy in El Paso, Texas, Oct. 15-17, Dr. Dominick J. Lacovara, chief, psychiatric program, Department of Health, Education and Welfare, U. S. Department of Justice, Bureau of Prisons, Federal Correctional Institution, Ashland, Ky., delivered a lecture on "The Abnormal Personalities" and was presented with a trophy by Mr. Homer H. Henry, attorney, Department of Justice, representing the Attorney General, in appreciation of his services.

MARYLAND

Society News.—Mr. John Sargeant, executive secretary, Medical and Chirurgical Faculty of the State of Maryland, has announced that effective Nov. 19, Dr. Everett S. Diggs, secretary of the Medical and Chirurgical Faculty, was succeeded in this post by Dr. William Carl Ebeling, Medical Arts Building, Baltimore 1.——At the annual meeting of the Maryland Academy of General Practice in Hagerstown Oct. 12, Dr. Joseph R. Guyther, of Mechanicsville, was elected president for 1959 and Dr. Walter A. Anderson, of Baltimore, president-elect.

MONTANA

Meeting Date Changed.—The 1959 interim session of the Montana Medical Association will be held in Helena on April 3-4 rather than on March 27 and 28 as previously announced. This change in the dates of the interim session became necessary when it was discovered that March 27 was Good Friday and March 29, Easter Sunday. Earlier dates in Helena were not available because of the legislative session and other conflicts. Montana physicians are urged to mark the new dates on their calendar.

Society News.—The Montana Society of Neurology, Psychiatry and Neurosurgery at its annual business meeting on Sept. 12 elected Dr. Wayne M. Roney, Billings, president; Dr. H. Ryle Lewis, Missoula, vice-president; and Dr. Martin A. Ruona, Billings, secretary-treasurer.——The Montana Chapter of the American College of Surgeons has elected Dr. David J. Almas, Havre, president. Dr. Arthur J. Movius, Billings, was named vice-president; Dr. Harry W. Power, Great Falls, secretary-treasurer, and Dr. L. L. Howard, Great Falls, councilor.

NEW YORK

Project to Improve Hospital Standards.—New York State's Department of Social Welfare has contracted with the Sloan Institute of Hospital Administration of the Graduate School of Business and Public Administration at Cornell University for the development of proposed standards to improve the regulation and supervision of the state's 410 hospitals. Mr. Robert A. Anderson, assistant director of the Sloan Institute, will serve as principal consultant for this project. It is expected that the Sloan Institute's report will be completed by Oct. 1.

Close Tuberculosis Hospital.—The closing of the Newton Memorial Hospital at Cassadaga, Chautauqua County, effective Dec. 31, was announced by Dr. Herman E. Hilleboe, state health commissioner. The tuberculosis hospital has a capacity of 104 beds. It has been operated by Chautauqua County for the care of tuberculosis patients since 1920. Chautauqua County officials have no immediate plans for using the hospital for other purposes. The announcement of Dr. Hilleboe followed receipt of an application from the Chautauqua County Board of Supervisors to close the hospital. Tuberculosis hospital care for residents of Chautauqua County will be provided at the State Health Department's J. N. Adam Memorial Hospital at Perrysburg. Out-patient services in Chautauqua County will be conducted by Dr. Walter E. Lawrence, superintendent of Newton Memorial Hospital.

New York City

Dr. Buckstein to Speak at Radiological Meeting.—Dr. Jacob Buckstein, assistant professor of clinical medicine, Cornell University Medical College, will present "Tumors of the Small Intestine—Clinical and Roentgenological Aspects" at the Kings County Radiological Society meeting, March 26, 9 p. m. in the Kings County Medical Society Building, 1313 Bedford Ave., Brooklyn.

Conference on Vaginal Diseases.—The New York Academy of Science is sponsoring a conference on "The Vagina" April 10-11, 9 a. m. to 5 p. m., at the Barbizon Plaza, New York City. Only fundamental aspects of vaginal diseases will be considered. Therapy will not be included. Interested physicians, if nonmembers of the academy, should write to the executive director of the academy, 2 E. 63rd St., New York City, for programs which will serve as tickets of admission. There is no registration fee.

Dr. Kanner to Give Annual Lecture.—The Association for the Advancement of Psychoanalysis has announced that the Seventh Annual Karen Horney

Lecture will be given by Dr. Leo Kanner, professor of child psychiatry, Johns Hopkins University School of Medicine, Baltimore, on "Centripetal Forces in Personality Development." The meeting will be held on March 25, 8:30 p. m., at Hosack Hall, at the New York Academy of Medicine, 3 E. 103rd St. A dinner honoring the guest speaker will precede the lecture.

OHIO

Dr. Peterson to Give Freedman Lectures.—On April 11 and 12, Dr. Harold O. Peterson, director, department of radiology, University of Minnesota Medical School, Minneapolis, will deliver the 11th annual Joseph and Samuel Freedman Lectures in Diagnostic Radiology at the University of Cincinnati College of Medicine. There will be no charge for the lectures. Radiologists desiring to attend are requested to write Dr. Benjamin Felson, X-ray Department, Cincinnati General Hospital.

PENNSYLVANIA

Philadelphia

New Research Wing.—Ground was broken on Dec. 9 for the new 2-million-dollar wing of the Woman's Medical College, Philadelphia. Twelve professors, the heads of the departments to be located in the new wing on its completion in 1961, broke ground for the five-story addition to be erected at the northeast corner of the college. The new wing, planned primarily for research, will provide laboratories and other facilities for the college's expanding research program. One entire floor will be reserved for teaching, and space will be allocated for diagnosis and treatment of patients. Corridors on each floor will connect with the college. The project is the third major expansion undertaken by the Woman's Medical College since moving to its present building in 1930. The research wing is being financed by a grant of $500,000 from the federal government, contributions from charitable foundations, industry, and friends of the institution, including its National Board, auxiliary groups, and alumnae.

PUERTO RICO

Temple Alumni Seminar.—The Puerto Rico Chapter of the Temple University Medical Alumni Association will be host at a postgraduate medical seminar to be held in March in Puerto Rico. Medical School alumni, physicians, and friends will leave International Airport, Philadelphia, March 7 for a week of study and pleasure in San Juan. The project, under the direction of Dr. George E. Mark Jr., will include a scientific program covering practical material for those in general practice. The lectures will be divided between Temple University medical faculty and Puerto Rico Medical School faculty. Highlights of the week will include a trip to the Virgin Islands, a tour of San Juan, outdoor barbecue and water show, banquets, and cocktail party. For information write Temple University Medical Center, Broad and Ontario Streets, Philadelphia 40.

VIRGINIA

Hospital Spring Congress.—The Gill Memorial Eye, Ear and Throat Hospital, Roanoke, will hold its 32nd annual Spring Congress in Ophthalmology and Otolaryngology and Allied Specialties, April 6-11, 1959. Among the guest speakers invited to attend are:

Drs. Joseph P. Atkins and Francis P. Furgiuele, Philadelphia; Walter S. Atkinson, Watertown, N. Y.; Kenneth D. Bailey, Fairmont, W. Va.; William L. Benedict and Bayard T. Horton, Rochester, Minn.; F. Willson Daily and Edgar N. Weaver, Roanoke; Windsor S. Davies and Albert D. Ruedemann, Detroit; Jeff Davis, Robin M. Rankow, and Jules G. Waltner, New York City; Wendell L. Hughes, Hempstead, N. Y.; John H. King, Washington, D. C.; George T. Nager and Walter L. Winkenwerder, Baltimore; Kenneth L. Roper, Chicago; and Russell A. Sage, Indianapolis.

Dr. Thomas K. Lyle, of London, England, has also been invited as a speaker. For information write Dr. Elbyrne G. Gill, 711 S. Jefferson St., Roanoke, Va.

GENERAL

Meeting on Surgery of the Hand in Chicago.—The 14th annual meeting of the American Society for Surgery of the Hand will be held Jan. 23-24 at the Palmer House, Chicago. Of the 13 papers to be presented, the following are by foreign authors:

Primary Repair of Flexor Tendons in the Digital Sheath, Dr. Claude Verdan, Lausanne, Switzerland.
The Study of Flexor Tendons and Their Coverings in the Process of Repair, Dr. Martin Entin, Montreal, Canada.
Objective Methods of Evaluating Hand Sensation and Its Use in Reconstructive Surgery, Dr. Erik Moberg, Gothenburg, Sweden.

A symposium on "Acute Trauma to the Hand and Its Complications," the morning of Jan. 24, will be moderated by Dr. William H. Frackelton, Milwaukee. All members of the medical profession are welcome. Registration fee is $7. For registration and information, write Dr. George S. Phalen, 2020 E. 93rd St., Cleveland, Secretary-Treasurer.

Methodist Hospital Association Convenes in St. Louis.—The National Association of Methodist Hospitals and Homes will hold its annual convention Jan. 27-29 at the Sheraton-Jefferson Hotel, St. Louis, under the presidency of Harold E. Baker, Chula Vista, Calif. The keynote address at the first general assembly will be given by Dr. George W. Crane, Chicago, on "Psychology Applied to Health and Welfare Organizations." Themes for the various section meetings include:

Charting New Routes to Better Patient Care.
Bringing Us Up-to-Date.
A Family Conference in Methodism.

Adding Zest to the Added Years.
Meeting Administrative Problems.
Long Range Planning.
Strengthening of Church Sponsorship and Improvement of the Quality of Care in Methodist Homes.
Consideration of the Psychological and Emotional Reactions of Young Women Living in these Homes.
The Task of Institutional Promotion and Fund Raising.

On Jan. 30, hospital personnel will join with the American Protestant Hospital Association in interdenominational meetings on "Homes for Aging" and "Homes for Children." For information write the Board of Hospitals and Homes of the Methodist Church, 740 Rush St., Chicago 11.

FOREIGN

Congress of Health Technicians in Paris.—The sixth Congress and International Exhibit of the Technicians of Health (physicians, laboratory chiefs, pharmacists, etc.) will take place June 9-12 in Paris at Parc des Expositions, Porte de Versailles. The main theme of the reports to be delivered is: "The Conditions of Life of the Patient in the Nursing Institute of the Future; The Role Performed by the Team of Health Technicians." The congress will be framed by the first large hospital exhibit made in France. For information write to the Secretariat of the Congress, 37, rue de Montholon, Paris 9°, France.

EXAMINATIONS AND LICENSURE

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MEDICAL SPECIALTY BOARDS

American Board of Anesthesiology: *Oral.* Phoenix, April 5-10. All applications already on file. Sec., Dr. Forrest E. Leffingwell, 217 Farmington Ave., Hartford 5, Conn.

American Board of Dermatology: *Written.* Several Cities, Oct. 5. *Oral.* Oklahoma City, Jan. 15-18, 1960. The final date for filing all applications is July 1, 1959. Sec., Dr. Beatrice M. Kesten, One Haven Ave., New York 32.

American Board of Internal Medicine: *1959 Schedule—Written,* Oct. 19. Final date for filing application is May 1. *Oral.* For candidates in the South and Southwest, New Orleans, Feb. 3-6. Final date for filing application was Jan. 1. *Oral.* For candidates in the Midwest. Chicago, April 15-18. Final date for filing application was Jan. 1. *Oral.* For candidates on the West Coast. Final date for filing application is March 1. *Oral.* For candidates on the East Coast, Nov. 6-7, 9-10. Final date for filing application is March 1. *Examination in the Subspecialties. Gastroenterology.* Philadelphia, April 17-18. Final date for filing application is Feb. 1. Sec.-Treas., Dr. William A. Werrell, One West Main St., Madison 3, Wis.

American Board of Neurological Surgery: Examination given twice annually, in the spring and fall. In order to be eligible a candidate must have his application filed at least six months before the examination time. Sec., Dr. Leonard T. Furlow, Washington University School of Medicine, St. Louis 10.

American Board of Obstetrics and Gynecology: *Oral and Clinical.* Chicago, May 8-19. Formal notice of the exact time of each candidate's examination will be sent him in advance of the examination dates. Candidates who participated in the Part I examinations will be notified of their eligibility for the Part II examinations as soon as possible. Sec., Dr. Robert L. Faulkner, 2105 Adelbert Road, Cleveland 6.

American Board of Ophthalmology: *Written,* qualifying test (*Part I*), Various Cities, Jan. 26. *Oral.* Philadelphia, June 2; St. Louis, Oct. 6-10. Sec., Dr. Merrill J. King, 22 White St., Rockland, Maine.

American Board of Orthopaedic Surgery: *Part I.* Washington, D. C., Denver, Colorado and Rochester, Minn., Mar. 26-27. Deadline for filing application was Nov. 30. *Part II.* Chicago, Jan. 21-23, 1959. Deadline for receipt of applications was Aug. 15. Sec., Dr. Sam W. Banks, 116 South Michigan Avenue, Chicago 3.

American Board of Otolaryngology: *Oral.* Chicago, Oct. 5-9. Final date for filing application is February. Sec., Dr. Dean M. Lierle, University Hospitals, Iowa City.

American Board of Pathology: Boston, April 16-19. Final date for filing application is Feb. 28. Sec., Dr. Edward B. Smith, 1100 W. Michigan St., Indianapolis 7.

American Board of Physical Medicine and Rehabilitation: *Written, Part I,* and *Oral, Part II.* Philadelphia, June 12-13. Final date for filing application is February 15. Sec., Dr. Earl C. Elkins, 200 First St., S. W., Rochester, Minn.

American Board of Plastic Surgery: *Oral and Written.* Boston, May 9-11. Final date for submitting case reports is Jan. 1. Corresponding Secretary, Miss Estelle E. Hillerich, 4647 Pershing Ave., St. Louis 8, Mo.

American Board of Preventive Medicine: *Written. Public Health.* Regional, Apr. 9-11. *Occupational Medicine.* Chicago, Apr. 17-19. *Aviation Medicine.* Los Angeles, Apr. 24-26. Final date for filing application for all three examinations is Jan. 15. Sec., Dr. Tom F. Whayne, 3438 Walnut St., Philadelphia 4.

American Board of Proctology: *Oral and Written.* Philadelphia, September. Final date for filing application is March. Sec., Dr. Stuart T. Ross, 520 Franklin Ave., Garden City, N. Y.

American Board of Psychiatry and Neurology: New Orleans, Mar. 16-17. Training credit for full time psychiatric and/or neurologic assignment in unapproved military programs or services between the dates of Jan. 1, 1950 and Jan. 1, 1954 was terminated on Jan. 1, 1959. Sec., Dr. David A. Boyd, 102-110 Second Ave. S. W., Rochester, Minn.

American Board of Radiology: *Special Examination.* Cincinnati, Mar. 16-19, 1959. Final date for filing application was Nov. 1. Candidates completing training June 30, 1959 are not eligible for the Spring 1959 examinations. Sec., Dr. H. Dabney Kerr, Kahler Hotel Bldg., Rochester, Minn.

American Board of Surgery: *Written* examinations (Part I) will be held on December 2, 1959 at various centers to be announced later. Candidates are urged to apply several months before completion of training requirements although the closing date for filing applications is August 1. Those completing training requirements after September 30 cannot be considered for the Part I examination in December of the same year. *Part II.* New Haven, Conn., Feb. 9-10; Durham, No. Car., March 9-10; San Francisco, April 13-14; Indianapolis, May 11-12; Columbus, Ohio, May 14-15. Sec., Dr. John B. Flick, 1617 Pennsylvania Blvd., Philadelphia 3.

Board of Thoracic Surgery: *Oral.* Los Angeles, April. Final date for filing application is Dec. 1. Sec., Dr. William M. Tuttle, 1151 Taylor Ave., Detroit 2.

American Board of Urology: The oral will be given in Chicago in February 1959. Sec., Dr. William Niles Wishard, Jr., 30 Westwood Road, Minneapolis 26.

GOVERNMENT SERVICES

AIR FORCE

Colonel Steinkamp Awarded Medal.—Lieut. Col. George R. Steinkamp, chief, Department of Astroecology, Division of Space Medicine, School of Aviation Medicine, has been awarded the Air Force Commendation Medal. The citation stated in part: "Colonel Steinkamp distinguished himself by meritorious service to the United States from September 3, 1955, to August [illegible], 1957. During which period, his leadership, exemplary foresight, and ceaseless efforts were instrumental in the resolution of many problems of major importance to the Air Force." Among his other decorations are the Bronze Star Medal and the European campaign ribbon with four battle stars.

Last February, Colonel Steinkamp, then chief of the department of space medicine, was in charge of the "sealed cabin" experiment involving A/1C Donald G. Farrell who spent seven days in the cramped cabin completely sealed off from contact with the outside world.

Commissioned in the Army medical corps in 1942, Dr. Steinkamp went directly overseas, serving in Egypt, Libya, Tunisia, Sicily, England, France, and Germany. After the war, he practiced medicine in Little Rock, Ark., for four years. When the Korean conflict broke out, he was recalled to active Air Force duty.

ARMY

Civilian Service Award.—Dr. C. Blanchard Henry, chief, Surgical Branch, Department of Military Medicine and Surgery, Army Medical Service School, has received the Meritorious Civilian Service award in a ceremony at Brooke Army Medical Center, Fort Sam Houston, Texas. The citation reads, in part, "Dr. Henry has rendered meritorious service by his personal dedication to improving the principles and practice of military medicine. Through his efforts many improvements in teaching facilities and instructional material in the field of combat surgery have been introduced." Since the authorization of the award in 1952, six such presentations have been made at Brooke Army Medical Center. Dr. Henry was in private practice of surgery in New York State until he entered the Army in 1942. He served as chief surgeon with field hospitals in France, Central Europe, the Philippine Islands, Japan, and Korea and was retired with the rank of Colonel. He assumed his present position in March, 1953.

NAVY

Two New Rear Admirals.—Rear Adm. Allan S. Chrisman, M. C., and Rear Adm. Calvin B. Galloway, M. C., were appointed to their present ranks on Dec. 1, 1958, filling vacancies created by the retirements of Rear Adm. French R. Moore and Rear Adm. Ocie B. Morrison Jr.

Rear Admiral Chrisman, a [illegible]-year veteran, is presently serving as Commanding Officer of the U. S. Naval Hospital, San Diego, Calif. With his appointment to flag rank he simultaneously assumed additional duty as District Medical Officer of the Eleventh Naval District with headquarters in San Diego. Rear Admiral Galloway, also a [illegible]-year veteran of active naval service, is under orders to report to the Bureau of Medicine and Surgery, where he will be the Assistant Chief of the Bureau for Research and Military Medical Specialties.

Retirements.—Rear Adm. French R. Moore was placed on the retired list on Dec. 1, 1958, after completing more than [illegible] years active naval service. He was Senior Medical Officer of the Marines at Guadalcanal and Division Surgeon, Second Marine Division, Tarawa, before returning to the United States in February, 1944. For having been specially commended by the head of the executive department for his performance of duty in actual combat Rear Adm. Moore was advanced on the retired list to the rank of Vice Admiral.

Rear Adm. Ocie B. Morrison Jr. was placed on the retired list on Dec. 1, 1958, after completing more than 33 years active service. In 1944 he reported as Corps Surgeon for the First Marine Amphibious Corps in the Pacific and Asiatic Combat areas where he participated in the invasion of Guam, Palua, Okinawa, and the advanced party landings in Shanghai and Tientsin, China. He was awarded the Bronze Star Medal with Combat "V", the Legion of Merit with combat "V", and later the Gold Star in lieu of the Second Bronze Star Medal for "meritorious service" in the North China landings.

During the Korean Conflict he was assigned as Force Medical Officer on the staff of commander, Naval Forces, Far East. Again he was awarded a Gold Star in lieu of a second Legion of Merit. For having been commended by the head of the executive department for his performance of duty in actual combat Rear Admiral Morrison was advanced on the retired list to the rank of Vice Admiral.

Capt. Robert L. Gilman, M. C., was placed on the retired list on Dec. 1, 1958, having reached the statutory retirement age. A 17-year veteran of active service, he last served in the Office of the Chief of Naval Operations. Capt. [illegible] R. Wagner, M. C., was placed on the temporary physical disability retired list on Dec. 1, 1958 after completing 16 years active service. Capt. David H. McKeague, M. C., was placed on the temporary physical disability retired list on Dec. 1, 1958 after 15 years active service.

DEATHS

Allen, Kotz, New Orleans; Memphis (Tenn.) Hospital Medical College, 1901; specialist certified by the American Board of Otolaryngology; formerly on the faculty of Tulane University School of Medicine; veteran of World War I; associated with the Eye, Ear, Nose and Throat Hospital; died in the Charity Hospital Nov. 3, aged 83.

Aronovitz, Samuel Ⓜ Miami, Fla.; College of Physicians and Surgeons, Baltimore, 1911; died in Miami Beach Oct. 26, aged 70.

Barry, Ray Kent, Miami, Fla.; University of Buffalo School of Medicine, 1898; died Aug. 7, aged 81.

Barton, Charles Randolph, Forest Hills, N. Y.; Harvard Medical School, Boston, 1924; certified by the National Board of Medical Examiners; died in the Creedmoor State Hospital, Jamaica, Oct. 10, aged 57.

Bradbrook, Henry, Cat Spring, Texas; American Medical College, St. Louis, 1902; World War I veteran; died in the Brooke Army Hospital, Fort Sam Houston, Sept. 7, aged 90.

Brindley, Claunch Goldthwaite Ⓜ Borger, Texas; University of Texas School of Medicine, Galveston, 1933; member of the American Academy of General Practice; veteran of World War II; served as chief surgeon of the Gulf Coast Lines Railroad and chief physician for the Texas College of Arts and Industries in Kingsville; died in the Methodist Hospital, Houston, Oct. 22, aged 49.

Buser, John Robert, La Porte City, Iowa; St. Louis College of Physicians and Surgeons, 1907; died in the Schoitz Memorial Hospital, Waterloo, Oct. 23, aged 77.

Cain, William Noel, Lexington, Ky.; University of Louisville School of Medicine, 1919; died in the Good Samaritan Hospital Oct. 30, aged 62.

Connally, William Albert, Hebbronville, Texas; Louisville (Ky.) Medical College, 1893; died Sept. 6, aged 92.

Connor, Edward T., Clifton Forge, Va.; Leonard Medical School, Raleigh, N. C., 1899; died Oct. 8, aged 89.

Coon, George E., Milton, Wis.; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1898; Milton Township health officer many years; served as a trustee of Milton College and was director of Milton Junction State Grade School Board for six years; died in Janesville Oct. 26, aged 88.

Coulson, Sewell Briggs Ⓜ Waldron, Ind.; Central College of Physicians and Surgeons, Indianapolis, 1903; veteran of World War I; past-president of the Shelby County Medical Society; on the staff of the William S. Major Hospital in Shelbyville; died Oct. 22, aged 80.

Davis, Leonidas Carey Ⓜ Columbia, S. C.; Medical College of South Carolina, Charleston, 1930; interned at the Columbia Hospital of Richland County; died in the Columbia Hospital Oct. 30, aged 57.

Devitt, Ellis King Ⓜ Old Lyme, Conn.; Maryland Medical College, Baltimore, 1907; medical examiner, town health officer, school physician, and member of the board of education; past-president of the Old Lyme Chamber of Commerce; a trustee of the Deep River Savings Bank; veteran of World War I; died in the Lawrence Hospital, New London, Nov. 4, aged 78.

de Yoanna, Saverio Aurelia, Brooklyn; Medico-Chirurgical College of Philadelphia, 1914; veteran of World War II; formerly associated with the Veterans Administration; died Sept. 12, aged 69.

Forsyth, David Harley Ⓜ Terre Haute, Ind.; Indiana University School of Medicine, Indianapolis, 1909; for many years on the staff of St. Anthony Hospital, where he died Oct. 29, aged 81.

Fulkerson, George, Enfield, Ill.; National University of Arts and Sciences Medical Department, St. Louis, 1916; died Aug. 5, aged 75.

Fullerton, Reuel Matthias Ⓜ Bay Village, Ohio; Western Reserve University School of Medicine, Cleveland, 1924; for 17 years physician at the Lakewood (Ohio) High School; veteran of World War I; served on the staffs of the Fairview Park Hospital in Cleveland and the Lakewood (Ohio) Hospital, where he died Oct. 25, aged 62.

Gallatin, Herbert Hayse Ⓜ Kerrville, Texas; University Medical College of Kansas City, Mo., 1911; formerly associated with the U. S. Public Health Service, and for many years on the staff of the Veterans Administration Hospital; past-president of the Kiwanis Club; died in the Sid Peterson Memorial Hospital Oct. 31, aged 83.

Ⓜ Indicates Member of the American Medical Association.

Gill, John Louis, Altadena, Calif.; Medical Department of Tulane University of Louisiana, New Orleans, 1901; retired from the Veterans Administration Nov. 30, 1950; died Oct. 26, aged 77.

Glickman, Milton Ⓜ Los Angeles; Loyola University School of Medicine, Chicago, 1940; interned at the Los Angeles County Hospital; veteran of World War II; served with the city health department; died in Cedars of Lebanon Hospital Oct. 7, aged 43.

Gray, Charles Mickel Ⓜ Vineland, N. J.; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1904; died Oct. 26, aged 79.

Grosby, Hiram Herman Garzell, St. Louis; Howard University College of Medicine, Washington, D. C., 1901; died in the Jewish Hospital Sept. 21, aged 82.

Haley, James Farrar Ⓜ San Antonio, Texas; Medical Department of Tulane University of Louisiana, New Orleans, 1894; died in the Laurelwood Medical Hospital Oct. 4, aged 96.

Hammond, Edward Lee, Commander, U. S. Navy, retired, San Antonio, Texas; University of Pennsylvania School of Medicine, Philadelphia, 1935; specialist certified by the American Board of Psychiatry and Neurology, Inc.; member of the American Psychiatric Association; entered the U. S. Navy in 1938; retired April 1, 1952; died Sept. 17, aged 47.

Harris, Leo Clay Ⓜ Lawrenceburg, Tenn.; University of Tennessee College of Medicine, Memphis, 1913; died Sept. 19, aged 72.

Hauer, Hugo, New York City; Friedrich-Wilhelms-Universität Medizinische Fakultät, Berlin, Prussia, Germany, 1903; died Aug. 18, aged 84.

Hawkinson, Oscar Ⓜ Oak Park, Ill.; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1906; member of the American Psychiatric Association; formerly on the faculty of Loyola University School of Medicine; past-president of the Chicago Medical Society; served on the staffs of St. Anne's Hospital in Chicago and the West Suburban Hospital, where he died Nov. 1, aged 81.

Holbrook, James H., Paintsville, Ky.; Kentucky School of Medicine, Louisville, 1900; an associate member of the American Medical Association; for many years on the staff of the Paintsville Hospital, which he helped to organize; past-president of the First National Bank of Paintsville; died Oct. 12, aged 84.

Tebow, Louis Elliott Ⓜ Captain, U. S. Navy, Tamaroa, Ill.; born in Grayson, Ky., Aug. 24, 1910; University of Illinois College of Medicine, Chicago, 1941; service member of the American Medical Association; commissioned in the medical corps of the U. S. Navy in June, 1941, as a lieutenant (junior grade), and attained the rank of captain on May 1, 1956; served during World War II; during the Korean conflict while aboard the hospital ship USS Repose, earned the Korean presidential unit citation; served at Navy hospitals in Bethesda, Md., and Great Lakes, Ill.; formerly chief of surgery and executive officer of the U. S. Naval Hospital, Guantanamo Bay, Cuba; chief of surgery at the U. S. Naval Hospital in Memphis, Tenn., where he died Oct. 27, aged 48.

Tindal, Edward F. Ⓜ Muncie, Ind.; Medical College of Indiana, Indianapolis, 1897; died in the Ball Memorial Hospital Oct. 28, aged 89.

Tipps, Bill, Oklahoma City, Okla.; University of Oklahoma School of Medicine, Oklahoma City, 1956; interned at St. Luke's Hospital in Chicago; died Oct. 15, aged 28, while serving as a captain in the Air Force Reserve in England.

Todd, E. B. Ⓜ Graeagle, Calif.; Medical Department of Tulane University of Louisiana, New Orleans, 1910; practiced in Eureka, Nev., where he was county health officer; died in the Western Pacific Hospital in Portola Sept. 21, aged 75.

Wainscott, Clyde Otis, Pendleton, Ore.; Willamette University Medical Department, Salem, 1912; past-president of the Eastern Oregon Medical Society; veteran of World War I; served on the staffs of Good Shepherd Hospital in Hermiston and St. Anthony's Hospital; died Oct. 25, aged 72.

Ware, Ella, San Antonio, Texas; University of Texas School of Medicine, Galveston, 1899; for many years practiced in Stockdale, where on Oct. 24, 1954, she was honored at "Ella Ware Day"; died Oct. 29, aged 88.

Willis, Park Weed Ⓜ Seattle; born in Umatilla County, Ore., July 10, 1867; University of Pennsylvania Department of Medicine, Philadelphia, 1891; in 1902 member of the House of Delegates of the American Medical Association; founder and past-governor of the American College of Surgeons; past-president of the Washington State Medical Association and the King County Medical Society; member of the Phi Beta Kappa, North Pacific Surgical Association, Seattle Surgical Society, and the Pacific Coast Surgical Association, of which he was past-vice-president; founder and first president of the Seattle Community Fund; in 1946 named president of the Pioneer Association of Washington State; for 50 years surgeon for the Northern Pacific Railroad; one of the founders and member of the staff of the Children's Orthopedic Hospital; on the original staff of the Seattle General Hospital; in 1951 received the Alumni Award of Merit from his alma mater and in 1945 the honorary degree of doctor of laws from the Whitman College in Walla Walla, where he was a trustee from 1909 to 1949; died Oct. 26, aged 91.

FOREIGN LETTERS

DENMARK

Enuresis.—In the children's department of a general hospital 167 children between the ages of 4 and 14 were treated for enuresis, with an average stay of 13 days in hospital. A follow-up examination one and one-half to three and one-half years after discharge from hospital by Dr. Grete Buchmann *(Nordisk medicin,* Oct. 16, 1958) showed that 25% were cured, 46% were improved, 25% showed no change, and 4% were worse. It is admitted that these results do not equal those claimed by some Americans who with the help of alarm clocks and other mechanical devices have achieved a cure in over 90% of their patients. The average stay of 13 days in hospital was shorter than the average for other Danish observers but doubt is expressed over the benefits of a longer stay. Indeed, the author concludes that it may be possible to treat enuresis on an outpatient basis if the pediatrician works in cooperation with a clinical psychologist. It is essential to indoctrinate the parents to assure a beneficial change of environment, and the school teacher to secure her sympathetic support.

Dextroamphetamine for Epilepsy.—A series of 160 epileptics was treated with dextroamphetamine by Dr. P. Hertoft *(Ugeskrift for læger,* Oct. 9, 1958). The drug was given by mouth in doses of 5 to 15 mg. once or twice a day, usually at 8 a.m. and 1 p.m. It was often unnecessary to exceed the initial dose of 10 mg. in one day. Such side-effects as nausea, anorexia, loss of weight, restlessness, sleeplessness, and drowsiness were slight, necessitating the abandonment of this treatment in only one patient. In the classification of the results of this treatment, the claim that it had been effective was reserved for those in whom there had been at least a 50% reduction in the frequency of the fits. The author concluded that dextroamphetamine is of great value not only in the control of epileptic fits, but also as a corrective to the depressant action of other drugs in common use against epilepsy. He has observed no addition to, or abuse of, this drug.

Prescalene Lymph Node Biopsy.—Since A. C. Daniels introduced prescalene lymph node biopsy in 1949, much has been learned about the lymphatic connections between the lungs and the paratracheal and cervical glands, and modifications have been made in the technique of this operation so as to increase its diagnostic value. In the past three years it has been practiced in the Odense City Hospital on 69 patients by Dr. P. Kölle-Jörgensen *(Nordisk medicin,* Oct. 9, 1958). The operation was carried out on the right side in 63 patients, on the left side in 4, and on both sides in 2. The patients could be roughly classified according as the histological findings were normal (31) or pathological (38). The normal specimens did, however, include one with anthracosis and 24 with "sinus catarrh." There had been clinical or radiological evidence suggestive of sarcoidosis in 38 patients, and among them there were 30 in whom the biopsy supported this diagnosis. Of the 38 specimens classed as pathological, the remaining 8 showed reticulosis, leukosis, etc. Complications after this operation were rare, but in one patient the phrenic nerve had probably been injured, and in two there was a somewhat prolonged serous secretion at the site of the operation.

Mitral Valvotomy.—Dr. Helge Baden reported a series of 167 patients who underwent mitral valvotomy. A follow-up examination of 108 survivors was carried out from 12 to 62 months after the operation, among them being 42 for whom it could be claimed that they were wholly or almost wholly rid of their cardiac symptoms. Excellent results were obtained in 33%, good results in 19%, fair results in 15%, no change in 11%, poor results in 6%, late death in 7%, and operative death in 9%. The frequency of good results rose with the postoperative size of the ostium, and the results were worse in association with regurgitation although there might be some degree of regurgitation among those with good results. To the question "Should symptomless mitral stenosis be operated on?" Baden says no. If symptoms should develop later, time will have been gained during which operative technique will have improved. Besides, some such patients may never develop symptoms.

Cancer of the Cervix.—Dr. Bent Sörensen (supplement 169 to *Acta radiologica*) reported a follow-up study of 798 patients who were treated with radium for cancer of the uterine cervix between 1922 and 1929. No other treatment had been used, and the dosage had been the same regardless of the age of the patient or the stage of the disease. All the 59 surviving in 1954 were contacted, and all the death certificates were studied with 12 exceptions. An additional six patients could not be traced. The death rate among the patients who had survived 5

The items in these letters are contributed by regular correspondents in the various foreign countries.

years after treatment was higher than among the population of the same age and sex as a whole, and the rate rose with the degree or extent of the disease at the time of the treatment, but this was not the case with the patients who survived 10 years or more. Late recurrences of the disease were responsible for 25% of all the deaths after the 5-year interval, and for 10% after the 10-year interval. The latest recurrence occurred nearly 27 years after treatment. The author concluded that patients need to be followed all their lives with the possibility of recurrence in mind.

INDIA

Artery Ligation in Hepatic Cirrhosis.—G. M. Phadke (*Indian Journal of Surgery*, vol. 20, August, 1958) subjected patients with portal hypertension caused by cirrhosis of the liver to a ligation of the hepatic, splenic, and left gastric arteries. Most of the patients were in the late stage of the disease with severe decompensation and ascites. Every patient was first put on medical treatment and the progress watched for six to eight weeks. The triple ligation was performed only on those who showed no improvement during this period with medical treatment alone. In the author's series of 62 patients with cirrhosis, 14 improved with medical treatment alone, 18 became worse or developed some complication, and 30 were operated on. After operation, ascites disappeared in 14 within a few weeks. Four who showed improvement in the immediate postoperative period later became worse and developed ascites, followed by death in two. Those who did not improve after the operation died within a year. Ten of the 30 severely decompensated patients enjoyed normal health three to six years after the operation. Those with ascites but without esophageal varices showed improvement both in the early and the late follow-up periods. Those with both ascites and varices had the highest mortality, only one of eight such patients being alive and well three years after the operation. There were only two patients with varices alone and both had attacks of hematemesis before operation. In one of them the attacks persisted after surgery, while the other who was having repeated bouts of hematemesis before operation did not have a single attack for about three and one-half years after surgery and was alive and well when last seen, although the varices were of the same magnitude. The presence of jaundice noticed either clinically or suspected by a high icterus index is a strong contraindication to this operation.

Adamantinoma of the Jaw.—Srivastava and Sikroria (*Indian Journal of Surgery*, vol. 20, August, 1958) described the clinical features observed in 17 patients with adamantinoma of the jaw. The youngest was 15 months old and, as the duration at that time was 10 months, the disease had started in this patient at the age of 5 months. The oldest patient was 36 years old, and 11 were below the age of 20. Almost all of the patients came from the middle or lower class. The duration of the tumor varied from two and one-half months to six years. The maxilla was involved in 3 and the mandible in 14. The teeth of the affected jaw were missing, loose, or displaced in all while ulceration and secondary infection, purulent discharge, and pain were present in nine. The diagnosis of adamantinoma could be made radiologically in only six patients, the others had a mistaken diagnosis of osteoclastoma, dentigerous cyst, or dental cyst. Three patients showed an unerupted tooth in the cystic cavity in the roentgenogram, and in one the roots of the teeth projected into the cavity. Three patients gave a history of previous operation. Partial resection of the mandible was performed on one and hemimandibulectomy on five. In one patient 75% of the mandible was removed after a preliminary course of deep x-ray therapy. Resection of the maxilla with suprahyoid dissection of the lymph nodes was performed on one patient. Curettage was performed on six, all of whom had cysts. In four the lesion was too advanced for operation and palliative deep x-ray therapy was given.

WHO Study Tour.—Five senior public health administrators from World Health Organization's (WHO) south east Asia region left New Delhi in October for Moscow on a six weeks' tour sponsored by WHO during which they will study public health administration methods in the USSR. They were joined in Moscow by 18 other participants from various countries. The group was led by Dr. J. Peterson, Director of the Division of Organization of Public Health Services at WHO headquarters in Geneva. The tour included visits to medical and health institutions in Russia, observation visits to work in the field carried out at different levels of government administration, and exchange of views on the spot with local and national health administrators.

Carcinoma of the Thyroid.—Shroff and Paymater studied a series of 108 patients with carcinoma of the thyroid (*Indian Journal of Surgery*, vol. 20, August, 1958). Since this series was taken from a total of 32,058 patients with carcinoma seen in the Tata Memorial Hospital, Bombay, incidence of this form of cancer was only 0.34%. There was also a preponderance in men (although the disease is more common in women) due probably to reluctance on the part of women to enter the hospital. In almost 70% of these patients the onset occurred between the age of 40 and 70 years. The histological variety in the younger age group was mostly a papillary carcinoma. The youngest patient in this study was a boy of 2 years and the oldest was a man of 78. In only 1 patient was carcinoma associated with symptoms of thyrotoxicosis, but 23 had nontoxic nodular goiter. In 24 of the patients in whom the carcinoma was evident clinically, as much of the growth as possible was removed and the residual disease was treated either with deep x-ray irradiation or with radon gold seeds inserted locally. Eight of these patients had no clinical evidence of disease five years after this treatment. Radical operation was possible in 11 patients on whom a total thyroidectomy and radical neck dissection, when there was evidence of cervical metastases, were performed. The authors recommended a prophylactic neck dissection only when the patient would not return for regular follow-up examinations and in patients with papillary carcinoma of the thyroid. For those who refused operation, and especially in elderly persons who had an anaplastic type of growth, radiotherapy alone was recommended. This was performed on 25 patients, in 7 of whom the disease remained controlled at the end of three years—3 of these were alive and well at the end of five years. The follicular variety was the commonest met with in this series.

Left Heart Catheterization.—Saini and Betts (*Indian Journal of Surgery*, vol. 20, August, 1958) catheterized the left heart in 11 patients, using the posterior percutaneous puncture technique. Patients who were clinically diagnosed as having lesions of both the mitral and aortic valves or double mitral lesions were selected for this investigation. Simultaneous right and left heart catheterization was performed on three patients. The left atrium was entered successfully in all patients, but the left ventricle could be entered in only three. Eight patients were subsequently subjected to cardiac operation and thus their findings could be correlated. Only two major complications were encountered. In one patient, about a foot of the catheter was cut off by the tip of the needle as it was being withdrawn, before removal of the needle. This was later removed surgically from the left atrium. Hemothorax in the right chest developed in another patient and was treated by aspiration and transfusion. Minor complications in six consisted of serosanguineous pericardial effusion in three and pleuritic pain for 24 to 36 hours in three. Pure mitral insufficiency could be diagnosed in two patients by this procedure, in one of whom it was proved at operation. Five patients in whom mitral regurgitation was suspected were found to have pure mitral stenosis and were later benefited by surgery. Only one patient with mitral insufficiency could not be diagnosed. Another with aortic stenosis was diagnosed by this investigation. One patient was diagnosed as having mitral insufficiency as the predominant lesion but this was not confirmed by operation.

Tetralogy of Fallot.—Betts and Gopinath (*Indian Journal of Surgery*, vol. 20, August, 1958) performed 50 operations on 47 patients with tetralogy of Fallot, the age of these patients varying from under 2 months to 21 years. They believed that from 4 to 10 years would be the optimal age for operative repair. Patients in whom the red blood cell count and hemoglobin level did not show a dangerous rise and who were under 4 years of age were seen every six months for examination and operation was delayed until a suitable age was reached. The authors preferred the Blalock-Taussig operation but went in on the side of the aortic arch rather than the opposite side as advocated by Blalock, so that a Potts-Smith aortopulmonary anastomosis could be performed if a subclavian-pulmonary artery anastomosis was not feasible. The first four operations in this study were the Potts-Smith type, and since then three other patients also had this type of anastomosis, one of whom was a child of 2 years of age whose aortic arch was placed too high and whose subclavian artery was not long enough for a Blalock operation. In the other two the subclavian artery was too small for an adequate shunt. From 1951 to 1953 the authors performed six operations but only one of the patients was still living. From 1954 to 1957 they performed 44 operations on 41 patients. One of these had an exploratory thoracotomy, another had an exploratory thoracotomy on the right side and a Blalock operation later on the left side, a third had a division of a subclavian artery arising from the ductus arteriosus. Of the 41 shunt operations, 3 were the Potts and 38 the Blalock type.

In most of the earlier Blalock operations, the subclavian artery was used after it had given off the first group of branches but later it was used before it gave off its branches, wherever this was possible. In those patients in whom a division was used, the improvement was not so striking as when the main subclavian artery was used before it divided and a larger shunt was established. The inferior pulmonary ligament was routinely mobilized and in some patients the perihilar tissues of the pulmonary hilum were sutured to the aortic adventitia to further relieve tension on the anastomotic line. A mild hypothermia was used in 1956 and 1957 in all these operations and this may have been beneficial. By the time the anastomosis was completed, the rectal temperature dropped to about 35 C (95 F). Rewarming was started as soon as the anastomosis was complete. The patient was kept in the operating room till the temperature was stabilized. No cardiac irregularities appeared with this mild hypothermia. The authors observed one serious complication in this series which has not been reported by others—loss of the left arm from ligation of the subclavian artery distal to its primary branches. The operation went on well but the left arm remained cold and blue after the operation and the patient, a boy of 15, was unable to move it. About 48 hours later a marked nephrotic syndrome developed and the arm had to be amputated. Recovery was good with increased exercise tolerance.

Several other patients complained of temporary pain or inability to move the arm properly for a short time. Three of the six early patients died within 48 hours of operation. A fourth lived just over two weeks and postmortem examination showed a complete transposition of great vessels and other anomalies. A fifth survived over a year with postoperative hemiplegia and died of subacute bacterial endocarditis. The last was still living. Of the later 41 patients there were two operative deaths and one late death. In one of the operative deaths, autopsy showed that the patient did not have a tetralogy of Fallot but an extremely marked infundibular pulmonary stenosis and an auricular septal defect, while the other had an additional valve cusp below the aortic valve. The late death occurred in a patient on whom the Potts operation was used and the shunt was too large. The case fatality rate was higher in patients of the younger age group; thus the authors had six patients under 3 years of age and three of them died, but in the age group 3 or over, there were 41 operations with 3 deaths, a case fatality rate of 7.3%. Most of the risk in young patients was due to the severity of the lesion itself, requiring operation at an early age. Of the 47 patients in this series the Potts operation was used in 7 and the Blalock-Taussig in 40. There was only one operative and no late death in the latter group, while none of the former survived.

Leprosy.—K. J. Randive and co-workers (*Indian Journal of Medical Sciences,* vol. 12, October, 1958) stated that the involvement of peripheral nerves and ganglion cells of somatic and autonomic origin appeared to be the most consistent feature of leprosy as revealed by histopathological study, the causative organisms exhibiting a particular disposition to migrate towards the sensory and sympathetic nerve fibers. In order to explore this phenomenon, the authors set up a series of tissue cultures and studied the response of human fetal spinal ganglia and skeletal muscle to Mycobacterium leprae under controlled conditions in vitro; 10-week to 20-week-old human fetal tissue, the source of both, was grown in solid plasma clot cultures in association with fragments of fresh lepromatous tissue. The cultures were stained with Zeihl-Neelsen stain within 72 to 96 hours of explantation of the lepromatous tissue. Control cultures of both types were stained by the same method. Of the spinal ganglion cultures grown with lepromatous tissue, 78% showed fibrocytes containing acid-fast material in some form, but only 7% of the cultures of skeletal muscle grown with lepromatous tissue showed acid-fast material in the fibrocytes. None of the control cultures of skeletal muscle showed such material in the fibrocytes, and among the control cultures of spinal ganglia a few rare fibrocytes in 7% showed faint acid-fast granules in the cytoplasm. Thus human lepra bacilli were attracted towards the spinal ganglion cultures and were then taken up by the fibrocytes. The nature of granules in the control spinal ganglion cultures could not be determined. The spinal ganglion fibrocytes also displayed strong phagocytic activity for the lepra bacilli, which was not observed in the fibrocytes of skeletal muscle.

Ergonovine Methyl Tartrate in Labor.—S. N. Garde (*Current Medical Practice,* vol. 2, September, 1958) stated that faulty management of the third stage of labor is the commonest cause of postpartum hemorrhage, which accounted for about 10% of all maternal deaths. The author injected 0.5 cc. of ergonovine methyl tartrate intravenously in the management of the third stage of labor. The injection was given in a series of 435 deliveries. The results were compared with those in a control series of 268. Of the 434 deliveries, excluding 1 involving placenta accreta, the longest duration of the third stage was 35 minutes and the shortest 90 seconds (average 7 minutes) and in the control series the longest duration was 30 minutes and the shortest 1 minute (average 8 minutes). The duration was thus probably slightly shortened by the routine use of this drug. The blood loss was also less in the treated series. The drug did not increase the incidence of manual removal of the placenta; there were two such cases in the treated series, one of which was the placenta accreta. In the control series there was one case of manual removal of placenta. The complication of hourglass contraction of the uterus was not observed in either series. The treated series included five cases of lower segment cesarean section. In these patients 1 cc. of the drug was given routinely when the uterine incision was made and the child was about to be removed. The average time required for complete separation of the placenta in normal cases was 76 seconds, while with a partially adherent placenta it was 3 or 4 minutes. No pressor effect was seen with the administration of this drug. During the puerperium, the initial retraction of the uterus was much better and the involution was quicker in the treated than in the control series. The drug also helped reduce the incidence of secondary postpartum hemorrhage. There was not a single patient with this complication in this series.

MEDICAL LITERATURE ABSTRACTS

INTERNAL MEDICINE

Peptic Ulcers in Rheumatoid Patients Receiving Corticosteroid Therapy. R. H. Freiberger, W. H. Kammerer and A. L. Rivelis. Radiology 71:542-547 (Oct.) 1958 [Syracuse, N. Y.].

An examination of the upper gastrointestinal tract in 114 patients receiving corticosteroid therapy for rheumatoid arthritis revealed peptic ulcers in 35 (or 31%). The incidence of ulcers appeared proportionately related to the dose of corticosteroids and to the severity of the arthritis. Thirty of the ulcers were in the stomach and 5 in the duodenum. Of the gastric ulcers, the great majority were in the antrum, 8 at the greater curvature. Ten of the ulcer patients had serious complications, both severe bleeding and perforation. Not only the antral location but also the roentgen-ray appearance of the ulcer was in many cases unusual. Particularly noteworthy was the flexibility of the stomach wall beneath and adjacent to the ulcer crater. The atypical appearance of a large number of these ulcers and the fact that the routine positions normally used in gastrointestinal examinations cannot be assumed by severely crippled patients can make detection of the lesions difficult.

Infectious Mononucleosis: An Analysis of 100 Cases with Particular Attention to Diagnosis, Liver Function Tests and Treatment of Selected Cases with Prednisone. W. R. Mason Jr. and E. K. Adams. Am. J. M. Sc. 236:447-459 (Oct.) 1958 [Philadelphia].

The etiology of infectious mononucleosis remains unknown, and controversy regarding its diagnosis continues. In their efforts to learn more about this disease, the authors tried to correlate their observations on patients seen at a college health center during the past 7 years. This report is based on an analysis of 100 cases with respect to clinical data, diagnosis, treatment, duration of illness, and complications. The analysis indicates a reasonable consistency of clinical and laboratory findings among these cases. Evidence is presented to suggest (1) that alterations of liver function are quite common and (2) that the usual hepatitis of infectious mononucleosis is probably different from that usually found in infectious and serum hepatitis. Treatment is generally symptomatic and supportive, and prolonged bed rest is usually unnecessary. A small, selected group of 17 patients was treated orally with prednisone, which appeared to initiate prompt symptomatic improvement, especially the lessening of pharyngitis. The hormone did not obscure the valuable laboratory signs, but also it did not appear to shorten the total duration of illness. The ultimate value of steroid therapy in this disease remains to be proved. It is the complications of infectious mononucleosis which, together with insufficient discrimination in the diagnosis, have given the disease the reputation of being protean.

Natural History of Asthma. R. S. B. Pearson. Acta allergol. 12:277-294 (No. 4-5) 1958 (In English) [Copenhagen].

The author reports on 625 patients with asthma who attended 2 London hospitals as outpatients over a period of 6 years. Asthma was considered to be primary in 553 of these patients and secondary to bronchitis in the remaining 72. There were 293 males and 332 females. Symptoms occurred before the age of 10 years in 261 patients (40.2%) and between the ages of 10 and 19 years in an additional 101 patients. In each succeeding decade, from 20 years onwards to over 60 years, the number of patients was falling to half the number of each preceding decade. There was a preponderance of boys over girls up to the age of 10 years, and a reversal of the ratio of males to females around puberty. A high proportion of the patients had a family history of asthma or other allergic diseases. The importance of allergic, infective, and emotional factors as observed by other workers was confirmed, and it was shown that 2 or 3 such factors were commonly present in the same patient. One hundred seventy-five patients (28%) were severely disabled, representing a higher ratio than what would be observed in general practice. This was confirmed by the large number of patients (102) who gave a history of status asthmaticus. It was observed that the proportion of severely affected patients rose with increasing age. Those in whom allergic factors alone were discovered were seldom severely disabled, but it was repeated-

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The place of publication of the periodicals appears in brackets preceding each abstract.

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ly noticed that infection of the bronchial tract or emotional stress exerted an unfavorable influence on the course of the disease. Of the 26 patients (14 males and 12 females) who died, 21 belonged to the group of severely disabled patients; 19 of these had a history of attacks of status asthmaticus, and 16 died in status asthmaticus.

The picture that emerges from these observations is, therefore, one of a constitutional disease manifested by an abnormally sensitive bronchial tract, which may be constricted by a wide variety of stimuli. Most of the cases commence in childhood or adolescence, and at this time allergic factors appear to play an important part. It is at this period of life that multiple manifestations of allergic disease are most often seen. Many patients probably undergo spontaneous improvements and perhaps recovery. Yet, as age proceeds, infection appears to play an increasingly important part, both in the precipitation and in the maintenance of asthma, and after the age of 40 years it may be associated with organic lung damage. It is not always easy to say on clinical grounds how often the infective attacks in asthma constitute a genuine bronchitis and how often they are confined to the upper respiratory tract. It is certain, however, that there may be little difference in the final aspect of the patient with primary bronchitis in whom attacks of asthmatic breathing occur and the patient with primary asthma in whom bronchitis occurs. As age increases, a higher proportion of patients are observed who have a persistently prolonged expiration and dyspnea on effort as well as during spontaneous attacks. A fatal outcome is rare in patients who are not severely disabled or whose asthma is purely allergic in origin, but death occurs not uncommonly in those with repeated attacks of status asthmaticus.

Treatment of Ambulatory Hypertensive Patients with Trimethidinium Methosulfate. R. A. Dunsmore, L. A. Dunsmore, A. Goldman and others. Am. J. M. Sc. 236:483-486 (Oct.) 1958 [Philadelphia].

Trimethidinium methosulfate is an asymmetric bis-quaternary amine which was used in the treatment of 50 patients with severe hypertension. Thirty-eight of these patients received the drug for a period of 3 to 11 months, that is, for a sufficient time to evaluate its efficacy. Treatment was begun by giving the drug in doses of 20 mg. before breakfast and 20 mg. at bedtime. In the absence of adequate blood pressure reduction, a third dose was added in mid-afternoon. Doses were increased by 20 mg. at each clinic visit until an optimum decrease in blood pressure was attained.

In a dose range of from 60 to 520 mg. daily, trimethidinium methosulfate was found to be an effective antihypertensive agent, the average diastolic fall being 32 mm. Hg. The condition of 37% of this group of patients was thus maintained with consistent normotensive levels, while 58% showed normotension but less consistently. In the remaining 5% of the patients the results were poor. The mechanism of action seems to depend chiefly on ganglionic blockage, although there are indications of an additional central action. Pharmacological side-effects are similar to those with other ganglionic blocking agents, with the exception that effects on the gastrointestinal tract appear markedly reduced. Reserpine and chlorothiazide were found to be synergistic with trimethidinium.

Low Serum Potassium Level in Severe Hypertension. T. Hilden and A. R. Krogsgaard. Am. J. M. Sc. 236:487-491 (Oct.) 1958 [Philadelphia].

A new clinical picture, termed "primary aldosteronism" or "Conn's syndrome," has been established in recent years. It is caused by overproduction of the highly active mineralocorticoid, aldosterone. The clinical picture is characterized by intermittent pareses, paresthesias, in some cases tetanic convulsions, polyuria, and hypertension. Aldosterone causes sodium retention and loss of potassium; this will give rise to a slightly increased serum sodium level with alkalosis and hypochloremia and, as the most important anomaly, a low serum potassium level. Since hypertension may be a feature of primary aldosteronism, the authors examined the serum potassium level in 32 patients with untreated essential hypertension. Normally the serum potassium level is between 3.5 and 5.6 mEq. per liter in 98% of persons. Low values were found in patients with severe hypertension. Of 14 patients, including 7 with papilledema, 4 had low normal values (3.5 to 3.8 mEq. per liter), and 5 had abnormally low values (below 3.5 mEq. per liter). During successful treatment with antihypertensive drugs the serum potassium rose to values of more than 3.8 mEq. per liter in the course of a few weeks to 3 months. The observed hypokalemia could not be ascribed to vomiting or diarrhea, nor could it be due to chronic renal disease or primary aldosteronism.

Observations in experimental and human hypertension support the view that adrenocortical function contributes to the pathogenesis of essential hypertension. A slightly increased aldosterone excretion has recently been found in patients with hypertension. The observed low serum potassium values may, therefore, be due to an increased production of aldosterone. As hypertension may be caused by primary aldosteronism, serum potassium determinations will become part of the routine investigation in severe hypertension. The authors feel that it is important to know that such patients may show low serum potassium values which are reversible on treatment and seemingly not due to adrenocortical disease.

Phenylbutazone Therapy in Patients with Rheumatic Disease and Coincidental Essential Hypertension. J. Zuckner, A. M. Ahern, O. Machek and C. Cariolo. Am. J. M. Sc. 236:460-465 (Oct.) 1958 [Philadelphia].

A large number of patients seen in arthritis clinics have coincidental essential hypertension. They are mostly elderly persons who are being treated for osteoarthritis. Phenylbutazone (Butazolidin) is one of the few drugs effective in the treatment of osteoarthritis. When hypertension is present, the benefits afforded by phenylbutazone are frequently denied because of fear of the consequences of sodium retention which occurs with this medicament. This study was conducted in order to determine to what extent phenylbutazone can be employed in these persons. Fifty-four patients (43 of them with osteoarthritis, 6 with rheumatoid arthritis, 3 with chronic bursitis, 1 with fibrositis, and 1 with disseminated lupus erythematosus and all with essential hypertension) were treated with phenylbutazone intermittently for periods up to 2 years. Satisfactory relief of rheumatic symptoms was obtained in two-thirds of the patients. Blood pressure was not significantly increased, and in no instance was it severe enough to require discontinuing therapy. No change in cardiac status resulting from phenylbutazone therapy was observed, but toxic reactions requiring cessation of this therapy occurred in 4 of 54 patients. The authors feel that patients with rheumatic disease and coincidental uncomplicated hypertension can be treated with phenylbutazone without special regard to blood pressure.

Diabetic Neuropathy Precipitating After Institution of Diabetic Control. M. Ellenberg. Am. J. M. Sc. 236:466-471 (Oct.) 1958 [Philadelphia].

Diabetic neuropathy has been assumed to be the result of poor diabetic control over a prolonged period of time. This conclusion has recently been challenged, at least in patients in whom the neuropathy presented as the initial clinical manifestation of diabetes and who had no signs or symptoms of uncontrolled glycosuria. The author presents on the basis of 4 case histories another deviation from the "poor control" concept of etiology. These cases illustrate the diabetic neuropathy that appears after the institution of control of the hyperglycemia and glycosuria with insulin and diet. Although insulin has been suggested by other workers as being the toxic etiological agent under these circumstances, the author cites several factors that seem to absolve it of this role. These are as follows: 1. The neuropathy precipitated by the institution of insulin control of diabetes is identical with all other forms of diabetic neuropathy as regards symptoms, signs, spinal fluid findings, and course. 2. The neurological picture tends to improve and even to disappear despite the continued use of insulin. 3. Control of the diabetes by measures other than insulin may also lead to the precipitation of neuropathy. Thus, insulin is not the noxious agent but acts as the medium for control of the diabetes which, in certain instances, leads to neuropathy.

Fatal Staphylococcal Infection. B. N. Purser. M. J. Australia 2:441-443 (Oct. 4) 1958 [Sydney].

The author reports on 31 male and 11 female patients, between the ages of 8 and 83 years, with fatal staphylococcic infection, who died at the Royal Prince Alfred Hospital in Sydney after periods of stay varying from 1 hour to 8 months and on whom autopsies were performed. Of the 42 patients, the fatal infection originated within the hospital in 18 and outside the hospital in 16; in the remaining 8 patients it is doubtful whether the infection was contracted at home or in the hospital. Of the first group of 18 patients, 7 died as the direct result of intravenous therapy; they included 5 with pyemia with or without endocarditis, 1 with acute endocarditis, and 1 with suppurative pneumonia. Three patients in this group died as a result of wound infection, 1 of these with pyemia and 2 with cerebral abscesses; 3 died of postoperative pneumonia, 3 of respiratory cross infections, and 1 of suppurative middle-ear disease from cross infection. There remains one patient in whom the mode of infection is doubtful, although he was treated with intravenous infusions. Of the 16 patients whose infections originated outside the hospital, 4 started as pyogenic skin infections; 12 infections probably commenced as staphylococcic respiratory infections.

According to the conclusions drawn by the author, there has been a marked rise in the death rate in Australia over the last 3 years from staphylococcic infection, and at the same time the number of cases of severe staphylococcic sepsis has been increasing. These findings are similar to those reported by workers in the United States. That the Staphylococcus organism can destroy tissue and kill patients with great rapidity was one of the most striking features in many of the cases in this series. However, that this is by no means a recent observation is shown by the report issued by Chickering and Park in 1919 on more than 300 deaths from staphylococcic pneumonia (J. A. M. A. 72: 617-626 [March 1] 1919). In some of the Australian patients bacteriostatic antibiotics appeared to lessen the virulence of the organisms, but in many patients massive doses of antibiotics, often in combination, appeared to have no effect whatsoever on the course of the infection. The fact that 7 patients died as a direct result of intravenous therapy points to the potential dangers of infusion procedures. These should be considered as surgical measures and performed in a strict aseptic manner.

Nasal Carrier Rate of Antibiotic-Resistant Staphylococci: Influence of Hospitalization on Carrier Rate in Patients, and Their Household Contacts. W. R. O. Goslings and K. Büchli. A. M. A. Arch. Int. Med. 102:691-715 (Nov.) 1958 [Chicago].

Cultures were taken from the vestibulum nasi of 587 patients on their discharge from the University Hospital in Leiden, The Netherlands, in an attempt to study the influence of antibiotic therapy on the frequency and the pattern of resistance in pathogenic staphylococci as present in the vestibulum nasi. At the moment of discharge about 40% of the patients were carriers of a penicillin-resistant strain of staphylococci; 30%, of a streptomycin-resistant strain; 25%, of a tetracycline-resistant strain; 9%, of a chloramphenicol-resistant strain; and 2%, of an erythromycin-resistant strain. Antibiotic therapy in the hospital promotes the colonization of resistant hospital staphylococci in the vestibulum nasi but is not a necessary factor. The total pattern of resistance of the colonizing staphylococci is mainly decided by the pattern of resistance of the Staphylococcus strain circulating in the hospital at that moment and only partly by the type of antibiotic therapy. The colonization, however, will happen by preference by a strain resistant to the antibiotic therapy given at that moment. Besides the influence of antibiotic therapy, there seems to be a private disposition of the patients, which also is of importance in deciding whether the patient will acquire hospital staphylococci in his vestibulum nasi.

The fate of the resistant staphylococci after the patients were discharged was followed up in 61 patients, as compared with the fate of sensitive staphylococci taken along from the hospital in 21 patients, and the course of the further carrier rate in 52 patients who left the hospital without pathogenic Staphylococcus organisms in the vestibulum nasi. After 6 to 12 months the carrier rate for pathogenic staphylococci and the resistance rate for penicillin had become normal, while resistance against chloramphenicol had disappeared completely. The rate for streptomycin and tetracycline resistance at that moment, however, was still higher than normal. The decrease in resistance against chloramphenicol was based partly on loss of the resistant strains but also in considerable part on loss of resistance while the strain itself stayed present in the patient. The decrease in resistance against the other antibiotics was, with a few exceptions for resistance against tetracycline, due only to loss of the resistant strains.

The spread of the resistant hospital staphylococci was studied in 455 family members and household contacts of 138 patients during a period of 6 to 12 months after discharge from the hospital. Transfer of resistant strains from the vestibulum nasi of discharged patients occurred in 8% of the family members and household contacts and in 11% of the families of those patients discharged with a resistant Staphylococcus strain. Figured on all discharged patients together, the percentages of transfer were 3% of the family members or household contacts and 4.5% of the families. In about 60% of the resistant staphylococci in the family members, the origin of the strain could be traced to direct or indirect contact with the hospital micro-organismal flora (hospitalization, visit to outpatient departments, visit to hospitalized relatives, and transfer from discharged patients). Antibiotic resistance in pathogenic staphylococci is mainly an epidemiologic problem.

Acute Hepatic Congestion as a Factor in Elevated Serum Glutamic Oxaloacetic Transaminase Titers Above 400 Units. L. H. Shields and R. E. Shannon. Am. J. M. Sc. 236:438-446 (Oct.) 1958 [Philadelphia].

There has been much discussion concerning the rise in levels of serum glutamic oxalacetic transaminase (SGOT) after myocardial infarction. Since glutamic oxalacetic transaminase is present in all human serums and in various tissues, particularly heart muscle, liver, skeletal muscle, and kidney (in descending order of concentration), sufficient necrosis of any of the above may cause a rise in SGOT levels. The authors point out that interest in unusually high transaminase levels and their possible association with acute congestive hepatomegaly was generated by the finding of an SGOT titer of 3,000 units in a patient with acute congestive failure without myocardial infarction or hepatitis. They investigated the SGOT levels of patients in the department of internal medicine in the Harrisburg (Pa.) Polyclinic Hospital. In the course of 1,900 SGOT determinations they discovered 29 patients who had SGOT titers of greater than 400 units.

The charts of these 29 patients were analyzed, and the following conclusions were reached: 1. Acute hepatic congestion can cause elevated SGOT titers. When the congestion is severe, titers above 500 units can result; when it is severe enough to cause hepatic necrosis, titers up to 3,000 units may occur. 2. The importance of the "hepatic congestion factor" in SGOT titers (above 400 units) is emphasized by the significant difference of the average titer in uncomplicated myocardial infarctions (482) and the average titer in all cases of acute hepatic congestion (1,042), irrespective of etiology. 3. Not infrequently, patients with acute myocardial infarctions may have SGOT titers greater than 400 units. 4. In patients with myocardial infarctions, titers above 650 units should lead one to suspect that functional hepatocellular injury, on a congestive basis, is concomitantly present. 5. Whereas high transaminase levels in myocardial infarctions not accompanied by liver congestion have no short-term prognostic value, high SGOT titers in myocardial infarctions associated with acute hepatic congestion presage poorly for the patient, and shock is more likely to complicate the clinical course.

The Results of 500 Percutaneous Renal Biopsies. C. Brun and F. Raaschou. A. M. A. Arch. Int. Med. 102:716-721 (Nov.) 1958 [Chicago].

Five hundred ten attempts at percutaneous renal biopsy were made on 406 patients with a variety of nephropathies at the Kommunehospitalet in Copenhagen between May, 1949, and January, 1958. The 510 attempts resulted in 268 renal biopsies which were suitable for histological examination. Satisfactory biopsy specimens were obtained in 106 (40%) of the 267 attempts with the patient in the sitting position and in 162 (67%) of the 243 attempts with the patient placed in the prone position, with a sandbag under the abdomen. The effectiveness of both methods has risen with increasing practice. The following complications were observed: Gross hematuria on the day of biopsy was observed in 7.9%, and hematuria persisting beyond the day of biopsy was observed in 6.6%. Blood clots in the urine were found in 19 cases, and ureter colic in 5 cases. A moderate retroperitoneal hematoma was seen in one case, but surgical intervention was not considered necessary. In 2.2% of the attempts blood transfusion was given after the attempt; in view of this, blood-group determination should always be carried out, and compatible blood should be available on each attempt.

In most of the patients the kidney function—expressed by endogenous 24-hour creatinine clearance—was unaffected by the renal biopsy. Only in 2 patients was the renal function briefly reduced after the renal biopsy, being due in both cases to ureter obstruction by blood clots. After removal of the clots the creatinine clearance quickly reached the initial value. Hemodialysis may be carried out after renal biopsy, but one should wait a few days after the biopsy before subjecting the patient to the heparinization necessary to the dialysis. Pain in the loins after the biopsy attempt was reported by 7% of the patients. Rise in temperature after renal biopsy was observed in 15 patients (3.6%); this is a rare sequela to biopsy, and its frequency has not even been raised in patients with pyelonephritis. There was no demonstrably higher incidence of macroscopic hematuria after renal biopsy in patients with uremia and hypertension than in patients without these symptoms. No deaths were observed among the 406 patients as a consequence of renal biopsy. So far only about 1,800 cases of attempts at renal biopsy have been published, and, therefore, it is too early as yet to compare the risks in liver biopsy and renal biopsy.

Malignant Reticuloendotheliosis (Letterer-Siwe Disease): Study of 2 Cases with Autopsy. F. Pedrón Puyou and T. Velázquez. Rev. invest. clín. 10:41-61 (Jan.-March) 1958 (In Spanish) [Mexico, D. F.].

Malignant reticuloendotheliosis (Letterer-Siwe disease) is a rare disease whose etiology is unknown. As a rule, it develops in young children (and rarely in adolescents) and runs a progressive course toward a fatal end. Diagnosis is made on biopsy of an enlarged lymph node, which shows typical hyperplastic reticuloendothelial cells transformed into pallid macrophages. The authors report on 2 girls, aged 4 and 13 years, respectively, with malignant reticuloendotheliosis who were observed at the Central Hospital in San Luis Potosi. Both patients complained of anorexia, weakness, pallor, fatigue, irritability, fever, and cough. The superficial lymph nodes were moderately enlarged but painless. There were a moderate leukopenia, anemia, and subcutaneous hemorrhages.

The first patient was hospitalized, after an illness of 2 weeks' duration, with acute abdominal pain in the splenic region, diffuse edema, hepatosplenomegaly, dyspnea, and progressive anemia which did not respond to blood transfusion and to administration of hematinic drugs. Roentgen-ray examination of the chest showed bilateral shadows of diffuse pulmonary infiltration similar to those of miliary pulmonary tuberculosis. Roentgen-ray examination of the cranial bones showed areas of rarefaction of the parietal and frontal bones, corresponding to the areas of alopecia. An histological diagnosis of malignant reticuloendotheliosis was made by biopsy of an enlarged inguinal lymph node. The administration of Aureomycin was ineffective. The patient died of marked anemia and acute dyspnea 1½ months after hospitalization. Autopsy showed diffuse macrophagic reticuloendothelial hyperplasia involving the internal and superficial lymph nodes, spleen, liver, lungs, kidneys, and other structures. There was a large subpial hemorrhage, and there was also a focal involvement of the myocardium, the scalp, some areas of the skin, and the bone marrow. The parietal and frontal cranial bones in the areas which corresponded to those of alopecia were as thin as if they were parchment. The histological picture of the cranial lesion was the same as that obtained from biopsy of an enlarged lymph node.

The second victim of malignant reticuloendotheliosis was observed twice during the course of her illness of 2½ years. She was hospitalized in the last stage of the disease, with acute hemorrhagic dermatitis of the face, lips, hands, and forearms, hemorrhagic lesions of the tongue, anemia, edema, ascites, and dyspnea. She developed acute symptoms of a staphylococcic infection; injections of cortisone and penicillin were ineffective. The patient died with symptoms of dyspnea and tachycardia and in a clouded state of mind. Autopsy showed, besides lymphatic, visceral, and other pathological lesions similar to those observed in the first case, chylous ascites, hemorrhagic lesions of the thoracic duct, acute necrosis of the duodenal wall, and hemorrhagic gastritis.

SURGERY

Surgical Experiences with Pulmonary Coin Lesions. O. V. Hibma and E. I. Boldon. Wisconsin M. J. 57:359-364 (Oct.) 1958 [Madison].

A pulmonary coin lesion is defined as "a solitary, rounded density as seen on x-ray, lying within the lung parenchyma, and without obvious origin from mediastinum, diaphragm, or chest wall." Surgeons who undertake the treatment of pulmonary coin lesions find themselves in general agreement that all, or nearly all, such lesions should be excised because of the possibility that the lesion may be cancer. If there is still disagreement, it centers about the proper course to follow in those lesions which show some calcification, a finding which in the past has been considered evidence of a benign process. The interest in the harmless-looking coin lesion lies in the fact that there is about a 37% chance that it represents malignancy. The chance of its being a primary bronchial carcinoma is about 30%.

The authors review observations on 24 patients with coin lesions, in 3 of whom diagnosis of carcinoma was established. They agree with those who recommend resection of all coin lesions, but they make certain specific exceptions. The presence of multiple, well-calcified lesions on x-ray constitutes satisfactory evidence of benignity. Lesions which are solidly calcified throughout seem to merit observation. Where previous films are available which show a partially calcified lesion, which has been stable over a period of at least one year, observation seems justified. This time interval is quite arbitrary, since Storey reported a case in which a partially calcified coin lesion remained stable for 6 years, then began to enlarge. Thoracotomy revealed primary adenocarcinoma. In dealing with coin lesions, an extensive examination is frequently unrewarding in establishing a diagnosis. The authors feel that the best diagnostic tool is exploratory thoracotomy. The surgeon and not time should establish the diagnosis.

Postoperative Course in Patients Who Had Undergone Mitral Commissurotomy. M. Alonzo. Riforma med. 72:1151-1155 (Oct. 11) 1958 (In Italian) [Naples].

In his review of commissurotomy performed on patients with mitral stenosis, the author found that patients, 20 to 40 years of age, had a better postoperative prognosis than younger or older patients. Female patients recovered better than male. A prolonged course of antirheumatic and cardiac supportive preoperative treatment was given to patients with an enlarged heart, a condition which could have been caused by the rheumatic myocardial lesions. Injection of alcohol into the intercostal nerves adjacent to the operative area during the operation decreased the intensity of postoperative pain. Thoracentesis of the pleural cavity was performed 48 hours after the operation. Transient dyspnea, moderate pericardial effusion, arrhythmia, and tachycardia were observed in the immediate postoperative period. The heart of the patient with nondecompensated mitral stenosis showed an excellent tolerance to intracardiac manipulation as compared with the poor tolerance of the heart of the patient with congenital disease of the myocardium or with a coronary disease. A sudden onset of tachycardia, which was the first response of the heart to its dilated cavities, was corrected by an intense therapy with digitalis and quinidine preparations during a period of 5 to 10 days. To prevent this disturbance, an uninterrupted preoperative and postoperative administration of small doses of quinidine was given routinely to all surgical patients with mitral stenosis. Recurrence of rheumatic symptoms, which developed in 2 patients within 20 days after operation, was controlled by an intensive antirheumatic therapy with salicylic acid preparations, aminopyrin, or corticotropin (ACTH). The characteristic cardiac murmur of mitral stenosis persisted in several patients after the operation despite the improved clinical picture, the regained physical strength, and the reduction of cardiac area. This incongruity can be related to the surgical operation, which corrects the hemodynamic state of the circulation but does not modify the pathological anatomy of the valvular cusps.

Contralateral Pleurisy After Thoracic Operations in Pulmonary Tuberculosis. H. D. Aguilar and J. C. Fernández. Rev. Asoc. méd. argent. 72:136-138 (April) 1958 (In Spanish) [Buenos Aires].

The development of contralateral pleurisy after a thoracic operation in a patient with pulmonary tuberculosis is rare. It is a new tuberculous lesion which occurs because of a lowering of the general and local immunobiological reactions. Constitutional and nutritional factors or such occasional conditions as pregnancy, infection, metabolic disorders, alcoholism, malnutrition, stress, or thoracic trauma may act as causal agents. As a rule, the disease develops suddenly, several months or maybe several years after the thoracic operation. The exudates are a serofibrinous liquid which roentgenologically resembles that of hydrothorax. The general pulmonary and extrapulmonary symptoms of contralateral pleurisy are the same as those in common serofibrinous pleurisy.

Out of 1,500 patients with pulmonary tuberculosis, who underwent thoracic operations at the Hospital Tornu in Buenos Aires, 3 patients, who ranged in age from 18 to 46 years, developed contralateral pleurisy. The illness occurred 8 months after a lobectomy in one patient and 4 months and 5 years, respectively, after a thoracoplasty in the other 2 patients. The treatment of 2 patients consisted of thoracentesis, followed by a regimen consisting of hygienic diet, the administration of calcium and tuberculostatic drugs, and bed rest; the same treatment without thoracentesis was given to the third patient. Corticosteroids were administered to all 3 patients at the end of treatment. The disease ran a favorable course, with reabsorption of the exudates within 2 or 3 months in all the cases. The patients have been followed up for 2 years, and they are now in good health.

Postoperative Acute Pancreatitis. D. Telford. Canad. J. Surg. 2:22-28 (Oct.) 1958 [Toronto].

The first of the 2 patients with postoperative acute pancreatitis was a 69-year-old man, in whom laparotomy confirmed the suspicion of chronic relapsing pancreatitis. Intraluminal exploration of the common bile duct revealed a stricture at its termination. This stricture was dealt with by transduodenal sphincterotomy. Postoperative progress was satisfactory for 24 hours. Then the patient became restless and complained of moderately severe abdominal pain. Within 12 hours the pain became excruciating, steady, and radiating. The return from the gastric suction was copious. The abdomen was tender, guarded, and silent. The differential diagnosis of postoperative complications included coronary thrombosis, rupture of the duodenotomy suture line, and acute pancreatitis. A serum amylase value of 64 units per 100 cc. (Windlow method) made the last diagnosis most likely. Treatment included administration of oxygen, fluids (intravenously), blood, and meperidine (Demerol) and continuous Levin tube suction, but the patient died. Autopsy revealed hemorrhagic pancreatic necrosis in the head and body of the pancreas, with extensive necrosis of the retroperitoneal and mesenteric fat. There was no obstruction to the ducts of Wirsung or Santorini.

In the second patient, a man, aged 50 years, the preoperative diagnosis of duodenal ulcer with penetration into the pancreas was confirmed at operation. Acute pancreatic edema developed in this patient. The most significant feature was the comparatively mild nature of the symptoms. The case demonstrates how easy it is for this entity to go unrecognized unless the disease is constantly kept in mind. Determinations of the serum and urinary amylase assist in the diagnosis and should be performed on the slightest suspicion of acute pancreatitis. Prevention is a challenge. Mobilization of the stomach, when there is a large gastric ulcer penetrating into the pancreas, requires special care. Sharp dissection is permissible down to the point where the stomach and pancreas are apparently inseparably fused, but beyond this point blunt dissection is to be preferred. Operation for duodenal ulcer may be traumatic to the pancreas. Deeply penetrating ulcer, associated with much periduodenitis, may have to be left intact.

The treatment of postoperative acute pancreatitis is usually medical. It must be compatible with other necessary postoperative measures. Frequent assessment of the patient's condition and willingness to adjust or supplement established therapy are important. Meperidine, which causes less spasm of the sphincter of Oddi than morphine, is the best drug for the relief of pain. If shock is present, meperidine is administered intravenously. Amyl nitrite may be of help if no shock exists. Procaine blocks may be employed. Supportive therapy includes the administration of fluids intravenously, also of electrolytes, blood, calories, insulin, antibiotics, and oxygen. Suppression of pancreatic secretion is advisable. Oral feedings are withheld, and nasogastric suction is established. An anticholinergic drug, such as methantheline (Banthine) bromide, is administered intravenously. Insulin is given to combat hyperglycemia, a condition which can cause overstimulation of the islet cells.

Surgical Correction of Defective Absorption of Vitamin B_{12} in a Child. W. C. Quinby Jr. and J. J. McGovern. New England J. Med. 259:755-760 (Oct. 16) 1958 [Boston].

Megaloblastic anemia due to vitamin B_{12} deficiency may occur in patients with lesions of the intestine, but the reviews of this subject include very few examples in infants or children. The present report describes the syndrome in a child. The girl was born with extensive ileal atresia and incomplete rotation of the cecum. She survived resection of the atresia with end-to-end jejunocolic anastomosis but showed malnutrition, maldevelopment, increasing abdominal distention, episodic diarrhea, and occult blood in the stools. Roentgenologic examination disclosed progressive enlargement of a jejunal segment proximal to the anastomosis. Resection and reconstitution of the jejunocolic anastomosis at 4 years of age was not beneficial. At 5½ years of age megaloblastic anemia due to vitamin B_{12} deficiency developed. The anemia responded to treatment with vitamin B_{12} administered intramuscularly, after which the enlarged jejunal loops were resected and the colon was reanastomosed to a normal-sized jejunum. Two areas of adhesion of the enlarged loops to the liver were the only obstructive mechanisms recognized at any time, and shallow mucosal ulcerations were found near one of them.

Now at 8 years of age the patient has shown improved nutrition, growth, development, and intestinal function. Diarrhea has subsided, and occult blood has gradually disappeared from the stool. Hematological values, including the serum vitamin B_{12} level, have remained normal for 27 months. Approximately 70 cm. of jejunum remains to provide function of the small intestine. Fecal-excretion tests with radiocobalt (Co^{60}) labeled vitamin B_{12} indicated that the greatly dilated segments of jejunum induced a megaloblastic anemia through interference with vitamin B_{12} absorption. The conclusion has been strengthened by the clinical and hematological improvement that followed excision of these segments.

Reversibility of Pregangrene in the Severely Ischaemic Limb. A. W. Humphries, V. G. Dewolfe and F. A. Lefevre. J. Bone & Joint Surg. 40A:983-993 (Oct.) 1958 [Boston].

Interference with blood flow to an extremity may be sudden or gradual. Sudden occlusion may result from an embolus, which generally arises within the heart, or it may result from the superimposition of thrombosis in situ upon an existing arteriosclerotic area of the artery. In either event sudden total occlusion of the main artery results in an ischemic limb. In certain instances lumbar sympathetic blocks may permit the development of enough collateral circulation to maintain the life of the limb, but usually collateral vessels do not have time to enlarge before death of the limb occurs and amputation must ensue. In these severely ischemic limbs early arterial surgery is imperative. This consists of embolectomy or thrombectomy, with repair of the vessel if the quality of the artery is good, or replacement of certain portions of it by arterial graft if the vessel is too sclerotic for repair.

Results of grafts in 71 consecutive patients with ischemic limbs are compared with a similar consecutive series of sympathectomies for ischemia performed prior to the advent of arterial grafting. Any procedure other than amputation represents a saved extremity. When looked at in this light, sympathectomy was a useful and efficient procedure, since only 38% of the 66 patients required amputation during a follow-up period of up to 7 years. The best results were obtained in patients who had only rest pain. The patients having ulcer, gangrene, and acute occlusion did not do well. In this series, 44% of the patients were improved and 18% remained the same, while in 38% amputation was done. This is a salvage rate of approximately 50%. Only 3 of 29 patients in whom definite improvement was obtained achieved normal limbs; the remaining 26 patients were relieved of rest pain, but all had claudication to some extent.

The follow-up period in the patients in whom grafting was done ranged up to 4 years. As in the sympathectomy series, the best results were obtained in patients with rest pain, since the arterial disease was not so far advanced as it was in the other groups. Of the 32 patients in whom improvement was gained in the group with rest pain, 26 had normal limbs, and only 6 still had claudication. This is essentially the reverse of the results in the sympathectomy group. Also, in the patients who had ulcer, gangrene, or acute occlusion, a much higher percentage of the patients not only retained their limbs but also did not have claudication; therefore, the number of amputations was much lower. In this series, 82% were improved (66% with normal limbs) and 6% remained the same, while in only 12% was amputation done. Also, with grafting the results in diabetic patients were essentially the same as in nondiabetic patients. The authors do not discount sympathectomy, feeling that it has a definite place in the treatment of the ischemic limb. Nevertheless, when arterial grafting can be accomplished, the results from grafting are far superior to those from sympathectomy.

Carcinoma of the Stomach. C. E. Welch and E. W. Wilkins Jr. Ann. Surg. 148:666-681 (Oct.) 1958 [Philadelphia].

From 1947 to 1956, inclusive, 637 patients with cancer of the stomach were admitted to the Massachusetts General Hospital in Boston. Palliative resections were carried out in 153 of the patients, with a mortality of 24%; and resections for cure were performed on 274 of the patients, with a mortality of 8.7%. The following percentages were the mortality rates in the various resections for cure: in subtotal distal resections, 8.2%; in subtotal proximal resection, 7.0%; in total gastrectomy, 14.5%; and in extended total gastrectomy, 15.4%. During the period from Jan. 1, 1947, to Jan. 1, 1953, 380 patients with carcinoma of the stomach were admitted. There were 49 who survived 5 years, of whom 7 are known to have died later of cancer. The over-all 5-year survival rate was 12.9%. The 5-year survival rate was 49% for those patients who had a distal subtotal gastrectomy and survived operation, 14% with proximal gastrectomy, 11% with total gastrectomy, and 18% with extended total gastrectomy.

Factors that affected this improvement in results include: (*a*) earlier diagnosis, particular attention being paid to those patients with supposedly benign ulcers, polyps, or pernicious anemia; (*b*) an increased number of operations; and (*c*) more radical resections, particularly for cancer involving other organs by direct extension. The most important factor in prognosis is the nature of the tumor itself. Size, location, penetration of serosa, microscopic appearance, and present or absence of metastasis are all of value in the determination of the prognosis.

It is suggested that cancers of the distal part of the stomach are treated adequately by subtotal distal resection, since 47% of those surviving such resections for cure were living 5 years later; furthermore, when lymph nodes had not been invaded, the 5-year survival rate was 63%. For large cancers of the cardia or entire stomach, the preferable operation appears to be total gastrectomy with splenectomy and hemipancreatectomy; however, the mortality rises with the extent of the procedure. Small cancers obstructing the cardia, particularly if they arise in a hiatus hernia, may be treated by proximal subtotal gastrectomy.

Treatment of Short Esophagus with Stricture by Esophagogastrectomy and Antral Excision. F. H. Ellis Jr., H. A. Andersen and O. T. Clagett. Ann. Surg. 148:526-536 (Oct.) 1958 [Philadelphia].

The authors use the term "short esophagus" to describe a condition in which the esophagogastric junction lies above the diaphragm and cannot be restored to its normal position below the diaphragm. In the vast majority of instances this condition follows a sliding esophageal hiatal hernia of long duration. Reflux of acid peptic juice into the esophagus leads to inflammation, fibrosis, shortening, and frequently stricture of the esophagus. A similar set of circumstances can be initiated by any operative procedure that destroys the esophagogastric junction and allows free regurgitation of acid peptic juices into the esophagus. At the Mayo Clinic, esophagogastrectomy and antral excision were done on 27 patients with esophageal shortening. The majority of patients also had esophageal stricture. The disease followed a sliding esophageal hiatal hernia in 24 patients and cardioplasty in 3.

One death occurred in the hospital after the operation. Two patients were operated on too recently for evaluation. The status of the remaining 24 patients was evaluated by reexamination in 18 and by letter in 6. All but one were relieved of their preoperative symptoms. When the over-all status of the patient was considered, 22 had a good or an excellent result. But 8 of these patients had some mild postoperative symptoms, and one or more of the following were present: nausea, vomiting, anorexia, regurgitation, and diarrhea. The regurgitation in one patient was so troublesome that he was classified as having only a fair result. Measurement of gastric acidity revealed that all the patients studied were achlorhydric after a test meal and after the administration of insulin; free acid was occasionally recovered after administration of histamine. Fecal excretion of fat was increased, an average of 15.1% of ingested fat being excreted over a 6-day period when patients were fed a diet containing 100 Gm. of fat daily. Esophagogastrectomy combined with antral excision is satisfactory for the treatment of certain patients with a short esophagus who fail to respond to medical management. A short esophagus with stricture is the chief indication for the use of this procedure. A less extensive operation may suffice in the absence of stricture, massive bleeding, or deep esophageal ulceration with destruction of the integrity of the esophagogastric junction.

Results of Three Methods of Therapy for Massive Gastroduodenal Hemorrhage: A Statistically Valid Comparison. K. E. Karlson, I. F. Enquist, C. Dennis and S. Fierst. Ann. Surg. 148:594-605 (Oct.) 1958 [Philadelphia].

The first of the 3 therapeutic methods selected for study was the nonsurgical regimen which included bed rest, feeding of a gelatin-milk mixture every 2 hours, and mild sedation. Transfusion was given only for air hunger and evidences of cerebral or myocardial hypoxemia or for blood pressure below 80 mm. Hg systolic, and then in 250 cc. amounts only. The second method was immediate operation. A three-quarter gastrectomy was undertaken in every patient in this group as soon as the patient had been evaluated and preoperative preparation had been accomplished. Transfusion should be continued until blood pressure and pulse are normal or until it is felt that a further improvement will not occur preoperatively. Preoperative preparation should not require more than 12 hours. In the third method, the selective operative regimen, several factors, such as age, the presence of arteriosclerosis, previous massive hemorrhage, and failure of transfusion, were considered in deciding on surgical treatment. All patients, 50 years of age or older, patients with severe arteriosclerotic changes in eyegrounds, the aorta, or peripheral arteries, and patients who had a history of previous hemorrhage from the stomach or duodenum sufficient to cause clinical shock were operated on immediately. In case of failure of transfusion to combat shock, patients were transfused with 1,500 ml. of whole blood as soon as possible, and, if shock persisted, transfusion was continued if possible, and operation was performed. The operation used in all cases was a 75% gastric resection with short loop, retrocolic Hofmeister-Pólya gastrojejunostomy.

Of 239 patients with upper gastrointestinal bleeding, 130 met all the criteria for admission to the "therapy group" and were managed by one of the 3 described methods. Fifty-eight were in the nonoperative group, 37 in the "immediate operative" group, and 35 in the "selective operative" group. The mortality rate was 14% in each of the 3 groups.

Although in this study the operative therapy for a single episode of massive upper gastrointestinal bleeding was identical with that of nonoperative therapy, the patient mortality might be lower in the operative group, because these patients are usually not subject to further episodes of massive bleeding, whereas those not operated on may have a recurrence of massive hemorrhage. No patient who lost less than 40% of the calculated normal total circulating red blood cell mass died of exsanguinating hemorrhage. This indicates that mortality figures based upon groups of patients who have lost less than 40% of their normal red blood cell mass are less significant than those based upon groups of patients who have lost at least 40%.

Technical Surgical Factors Which Enhance or Minimize Postgastrectomy Abnormalities. W. E. Abbott, H. Krieger and S. Levey. Ann. Surg. 148: 567-593 (Oct.) 1958 [Philadelphia].

The authors made studies on 15 normal volunteers and 85 patients, the latter having undergone gastric operations from 8 days to 7 years previously. The aim was to evaluate the changes in gastrointestinal function after various operations for the treatment of peptic ulceration. A barium-food mixture was prepared by adding food equivalent to an average breakfast to 75 Gm. of barium sulfate and mixing it in a blender. The food consisted of 60 cc. of orange juice, 60 cc. of coffee, a slice of toast with a pat of butter, a soft-boiled egg, and a pinch of salt. A roentgenogram of the abdomen was first made in the upright posture to ascertain the proper position for the visualization of the diaphragm and upper abdomen. Then the barium-food mixture was ingested, and upright films of the abdomen were obtained 1 minute later and after 10, 20, 30, 45, and 60 minutes. The patient was not permitted to lie down during this period. In most instances studies were obtained 8 to 12 days postoperatively and often from 3 months to 4 years later. Additional studies carried out in some of the patients included an oral glucose tolerance test, determination of plasma volume (while resting, after ambulation, and after ingestion of hypertonic glucose solution), of body weight changes, and of fecal nitrogen and fat (while the patient was on a constant diet). The daily caloric consumption was frequently determined, and, if anemia occurred, its type and cause were investigated.

Since recurrent ulceration is now comparatively rare after surgical treatment, attention should be focused on the avoidance of other sequelae. The authors found that as regards the rate of gastric emptying, although the size of the anastomotic stoma was important, the position and possibly the mucosal folds and other factors were also important. Often the function of the stoma cannot be correlated with the stomal size as estimated by the surgeon. Stomal function is best studied by roentgenographic methods. "Dumping" refers to rapid gastric evacuation, which may be associated with (*a*) anorexia that leads to a decreased food intake resulting in undernutrition, (*b*) vasomotor symptoms, and (*c*) diarrhea. Dumping and insufficient nutrition have been observed after gastroenterostomy and vagotomy and with subtotal gastrectomy and gastroduodenostomy or jejunostomy with and without vagotomy. In each instance the results could be correlated with the size of the stoma and the rate of gastric emptying, as shown by the barium-food x-ray studies. The best results were seen in patients who had a small stoma and a gastric emptying time approximating that of normal subjects. The internal diameter of the stoma should probably not exceed 2 cm.

Recent studies have shown that there are many factors which govern the presence or absence as well as the type and severity of symptoms associated with dumping. Distention and stasis in the stomach or afferent loop may produce symptoms that are comparable to those seen with dumping. The symptoms may be exaggerated when the patient assumes the recumbent posture. The barium-food study is helpful in differentiating the underlying cause. The following examinations are deemed necessary for complete evaluation of the results of the various operations: (1) rate of gastric emptying and small intestine transit time determined by roentgenography; (2) patient's daily caloric intake estimated by means of a weigh-back diet; (3) testing for postprandial hypoglycemia and latent symptoms associated with dumping by the oral administration of hypertonic glucose; (4) blood counts (should the patient be anemic, the cause should be determined); and (5) gastric analysis with histamine and/or insulin stimulation. The authors obtained the best results in patients who had a hemigastrectomy, vagotomy, and a small stoma gastrojejunostomy.

Pulmonary Resection for Tuberculosis Under Protection of Viomycin, Promizole and Pyrazinamide. W. R. Webb and K. Sparkuhl. Dis. Chest 34:484-495 (Nov.) 1958 [Chicago].

The authors report on 32 patients with pulmonary tuberculosis who had open positive lesions with bacilli proved or presumptively resistant to streptomycin, aminosalicylic acid, and isoniazid. Thirty-five pulmonary resections were performed on these patients, each patient being placed on viomycin in combination with thiazolsulfone (Promizole) or with pyrazinamide, a potent synthetic derivative of nicotinic acid, for a 2-week period preoperatively and for about 3 months postoperatively. The usual doses administered were 2 Gm. of viomycin twice a week, 1 Gm. of thiazolsulfone 4 times daily, and about 500 mg. of pyrazinamide 4 times daily. During this period streptomycin, aminosalicylic acid, and isoniazid in the combinations which the patients had been receiving were maintained for whatever value they might possess. It was thought that this group of patients became resistant to the original chemotherapy because of various mechanical obstructing factors which tended to keep cavities open. Hilar fibrosis and extensive peribronchial lymphadenopathy produced bronchiectasis, bronchostenosis, tension cavities, and carnified parenchyma. These would prevent cavity closure regardless of the nature or duration of antibiotic therapy employed and thus allow the development and persistence of resistant bacilli.

Of the 32 patients operated on, 4 died; none of the deaths was related to the resistant bacilli or drug status. One patient had a massive pulmonary embolus while on the operating table; a second died on the 20th postoperative day of pulmonary emboli proved by autopsy; the third death resulted from pulmonary circulatory insufficiency 6 days after resection; and the fourth patient died of myocardial failure with pulmonary edema on the first day after resection. There was no bronchopleural fistula, empyema, or postoperative spread. Of the 28 surviving patients who had been followed for from 6 to 36 months, 2 had an early and 1 a late reactivation. Three additional patients had late bacteriological relapses but have subsequently been negative for more than one year. Thus, 22 patients have never shown postoperative activity, and 26 may now be classified as arrested or inactive. Viomycin combined with either thiazolsulfone or pyrazinamide appears to offer satisfactory temporary protection for excisional surgery in patients with pulmonary tuberculosis. Nonetheless, thiazolsulfone has not been used since the availability of the more potent pyrazinamide.

Case of Infantile Ulcerative Colitis. I. Coll and D. L. Stevenson. Brit. M. J. 2:952-954 (Oct. 18) 1958 [London].

The authors report on a male infant who at the age of 3 weeks first showed symptoms of ulcerative colitis, i. e., persistent diarrhea, the fecal discharges containing blood and mucus. A barium-enema examination showed that the descending and proximal sigmoid portions of the colon were extremely irritable, resulting in rapid return of the enema. Filling of the colon was obtained only as far as the hepatic flexure. There was persistent spasm of the wall of the descending colon, and the mucosa of the sigmoid and descending colon appeared thickened. Sigmoidoscopy with the aid of anesthesia revealed a rectum half filled with blood-stained fluid. The mucosa was inflamed, but no ulcers were seen. Laparotomy, which was performed 3 weeks after admission to hospital, revealed the whole of the sigmoid colon as being dilated and thickened. A definitive diagnosis of ulcerative colitis, involving the descending colon, sigmoid colon, and proximal rectum, was made. No further operative procedure was carried out, but cortisone therapy was started, with a daily dose of 50 mg. as a preliminary measure, with the proviso that, if this therapy was not effective, resection would have to be carried out. Three months later there was no marked improvement, and when administration of cortisone was discontinued, the infant's health began to deteriorate rapidly. A resection of the left-sided third of the transverse colon, descending colon, and sigmoid colon with an end-to-end anastomosis was then performed. The patient made an uneventful recovery; 16 months after operation he had gained over 14 lb. (6.4 kg.) in body weight and was having 2 bowel movements a day without any blood or mucus.

Relationship of Polyps of the Colon to Colonic Cancer. J. S. Spratt Jr., L. V. Ackerman and C. A. Moyer. Ann. Surg. 148:682-698 (Oct.) 1958 [Philadelphia].

The concept that adenomatous polyps of the colon are precancerous growths is widely accepted. The evidence in favor of the concept is circumstantial and consists of (1) the detection of cellular populations within adenomatous polypoid masses in the colon that possess the histological characteristics of cancer and (2) the seeming concordance of the distributions of adenomatous polyps and of cancers in the colon, both being most numerous in the rectum and sigmoid and least numerous in the transverse colon. With regard to the location of cancer cells, polyps of the colon are of 2 types; in one the neoplastic cells are located in the stalk as well as in the body, and in the other they are located only within the polyp, the stalk not containing any. Although the type of carcinoma which is excluded from the stalk of the polyp may have all the histological appearances of cancer, it does not behave biologically as cancer. The authors studied records of 243 patients from whom single colonic cancers were removed at the Barnes Hospital, St. Louis, between June 1, 1952, and Dec. 31, 1955. Fifty-three of them had colonic adenomatous polyps in addition to the cancer, and 190 did not bear any polyps in the segment of colon removed and none were evident upon sigmoidoscopic, palpatory, and roentgenographic examinations of the remainder of the colon. The positions of all the polyps and carcinomas found within the colon were mapped.

The authors found that the frequency distributions of adenomatous polyps and cancers in the colon were not congruent. Adenomatous polyps were more evenly distributed throughout the colon than cancers were, and the unit percentile frequencies of cancers were higher than those of polyps in the cecum, sigmoid colon, and rectum and lower than those of polyps in the other parts of the colon. The frequency of cancer per unit length of cecum was the same as it was in the rectum and higher than it was in the sigmoid. Individual adenomatous polyps associated with colonic cancers were not randomly distributed above and below the respective cancers as they should be if colonic cancers had adenomatous polyps as their predominant loci of origin. In the right colon 20 of 26 polyps were located distal to their associated cancers, and in the rectum and sigmoid 68 of 92 polyps were located proximal to their respective cancers. The frequencies of occurrence of adenomatous polyps were the same in cancerous and noncancerous colons of persons over 50 years of age.

The locational frequencies of carcinoma of the colon in patients with familial polyposis were not different from those of cancers in colons without polyps. Among 425 adenomatous polyps 43 contained cellular populations having the microscopic appearance of cancer, with only one of the 43 having the abnormal cells questionably infiltrating the stalk of the polyp. Among 325 cancers of the colon no residuum of an adenomatous polyp was seen. These observations are not compatible with the theory that adenomatous polyps degenerate into infiltrating, metastasizing carcinomas of the colon. The observed frequencies of occurrence of minute infiltrating adenocarcinomas arising in nonpolypoid colonic mucous membranes are adequate to account for the annual incidence of carcinoma of the colon of 45 per 100,000.

NEUROLOGY & PSYCHIATRY

Circumstances Surrounding Complications of Cerebral Angiography: Analysis of 546 Consecutive Cerebral Angiograms. D. R. Coddon and H. P. Krieger. Am. J. Med. 25:580-589 (Oct.) 1958 [New York].

The authors review and analyze the circumstances surrounding the complications which attended 546 consecutive angiographies performed at Mount Sinai Hospital, New York, between July, 1952, and December, 1956. Of the 546 arteriograms, 530 were performed by the percutaneous technique. In the 16 remaining cases the common carotid was exposed and cannulated either because of failure to puncture the artery by the percutaneous method or because of contemplated ligation of the artery. The injections were of 10 to 12 cc. of 35% Diodrast, except for 6 injections of 50 to 100 cc. of 70% Urokon via the antecubital vein. These 546 procedures were performed on 483 patients. A complication is defined, for the purposes of this study, as any objective detrimental alteration in the patient's well-being within the first 24 hours after arteriography. A total of 109 complications occurred in this series. More than 90% were manifested during or just after the procedure. These complications occurred in 86 patients (17%), giving an over-all complication rate of 22% in relation to the total number of patients or 19% of the total number of arteriograms.

Two factors were chiefly associated with the occurrence of serious complications: (1) depression of consciousness and (2) progression of neurological signs. No relationship between the cardiovascular and hypertensive status of the patient and the occurrence of a complication was demonstrable. One-fourth of the patients with aneurysm suffered a serious complication; no apparent cause for this high rate was found. Of the nonfatal complications, 0.8% were permanent. In only one patient did death appear to be directly attributable to the procedure. In 7 cases the relation of the procedure to the ultimate death of the patient was probably not causal. Arteriography must be evaluated with regard to the incidence and severity of such complications. In this series 80% of the arteriograms gave diagnostically useful information. The authors conclude that in selected cases cerebral arteriography provides diagnostic information which outweighs the risk of complication.

Psychological Implications and Effects of Insulin Therapy. M. Rosenthal and L. A. Schwartz. J. Nerv. & Ment. Dis. 127:232-237 (Sept.) 1958 [Baltimore].

The studies described were designed to compare the relative effectiveness of deep-coma and subcoma insulin therapy in a clinical setting offering similar psychological and extra-treatment conditions. The use of the Multidimensional Scale for Rating Psychiatric Patients (MSRPP) offered an opportunity for symptom cluster analysis and made it possible to measure, in a relatively objective fashion, the areas of psychopathology for which insulin treatment was effective. This scale was used for pretreatment and post-treatment comparison. Twenty-seven hospitalized schizophrenic patients selected as suitable candidates for deep-coma insulin treatment were assigned randomly to either deep-coma or subcoma treatment. The authors found that the results of these studies provided further support for their previous research, namely, that subcoma is as effective as deep coma induced by insulin. Subcoma insulin treatment has a number of advantages over deep-coma insulin treatment. The possible risks involved are reduced considerably. Cooperativeness is more easily obtained, and the patient is more amenable to psychotherapy. Fewer contraindications to treatment exist, and personnel needs are reduced. Finally, the expense of treatment per patient is less.

The use of insulin coma therapy has fallen off considerably, and many psychiatric facilities no longer make it available. The results obtained by these authors indicate that benefit may frequently be obtained from subcoma levels of insulin. The results of the comparison of deep-coma and subcoma insulin therapy point increasingly toward an explanation of insulin effectiveness which includes the psychological conditions and impact of the total treatment setting. It is felt that the study confirms once more the effectiveness of insulin treatment in ameliorating schizophrenic symptoms and also demonstrates the usefulness of the MSRPP in measuring the psychological effects of a somatic treatment. It is suggested that it might be of considerable value to conduct controlled clinical studies with the various tranquilizing drugs, utilizing the MSRPP as one of the main instruments to evaluate the psychological effects of this type of somatic treatment.

GYNECOLOGY & OBSTETRICS

Vaginal Metastases of Endometrial Carcinoma. L. A. Arrighi and R. Inza. Semana méd. 65:351-354 (Aug. 21) 1958 (In Spanish) [Buenos Aires].

Two hundred twenty-six women with endometrial carcinoma were observed during the last 25 years at the gynecologic clinic of the University of Buenos Aires. Seventeen of these patients (7.5%) had vaginal metastases. The myometrium was already involved in all cases. In 10 patients the endometrial and vaginal lesions developed simultaneously. The vaginal metastases were multiple in 7 cases and solitary in 3. Multiple metastases were associated with metastases of the inguinal lymph nodes, the pelvic bones, and several other structures. The metastases occupied the lower third of the vagina in the majority of the cases. In 7 cases there were no metastases when the endometrial lesion was diagnosed. Metastases appeared between 6 months and 2 years after a total adnexohysterectomy. Simultaneously with late vaginal metastases there were metastases of the inguinal lymph nodes, the pelvis, and the vulva. Vaginal metastases appeared in all cases in the form of submucous nodules which underwent infiltration, granulation, and transformation into extensive bleeding ulcers.

Histological examination of the tumors and their metastases showed cylindrical carcinoma in 13 cases, nondifferentiated carcinoma in 2, and basal-cell carcinoma in 2. Three patients who were in advanced stage of endometrial cancer had no treatment. In the remaining 14 patients the treatment consisted of intrauterine and vaginal radium therapy or of adnexohysterectomy followed by roentgenotherapy. All the patients but 2 died within the first year after starting treatment. They died as a result of aggravation caused by metastases other than vaginal. The 2 survivors are living 10 years and 1 year, respectively, after treatment. The patient who has survived 10 years had a solitary vaginal metastasis complicating endometrial carcinoma. She had a total adnexohysterectomy followed by vaginal application of radium.

Sex Hormones and Mammary Cancer: Experience with Durabolin. J. T. van der Werff. Brit. M. J. 2:881-883 (Oct. 11) 1958 [London].

In recent years it has become clear that, after prolonged administration and even in cases which originally showed a favorable response, androgens in the end may stimulate tumor growth. This escapes observation because the impression is gained that the preparation has ceased to have effect. Recent research shows that the body is capable of gradually converting certain androgens into estrogens. This has long been suspected not only from the similarity in structure of the estrogenic and androgenic steroids but also from the fact that androgen therapy produced an increase in estrogen excretion. It is clear, therefore, that for prolonged administration a steroid is needed which does not show this conversion and yet possesses the favorable properties of the androgens used for the treatment of mammary carcinoma. Apparently the new compound, norandrostenolone phenylpropionate Durabolin, compares favorably with testosterone propionate, until now the most important hormone for use in mammary carcinoma. It seems that conversion of Durabolin into estrogen is not so easy, or is perhaps even impossible, so that there is a possibility for more prolonged administration. In addition, it has an anabolic effect 12 times more powerful than testosterone propionate, and the calcium excretion in patients with bone metastases can be greatly reduced after administration, while the virilizing effect is far less pronounced. The duration of action is long, so that weekly injections of 25 mg. are sufficient. The preparation is well tolerated, and patients who show a favorable response feel much better, acquire a good appetite, and look well.

Results obtained with Durabolin in 21 patients are presented. This group included 13 patients with such generalized metastases that recovery could not be expected, and 8 of these 13 have died. In 8 other patients the metastases were not yet very pronounced, but other conditions made the prognosis bad, and Durabolin was administered to improve this; all are still alive. In practically all the 21 patients considerable improvement in the general condition was observed. This became manifest in alleviation of pain (which was sometimes very severe as a result of bone metastases), in a good appetite, and in a general sense of well-being. Durabolin is usually a powerful and long-acting palliative which, owing to its slight virilizing action, is a real asset in the treatment of mammary cancer.

Hydatidiform Mole: A Report of 4 Cases. R. C. Evans. Arizona Med. 15:722-726 (Oct.) 1958 [Phoenix].

Hydatidiform mole is rare, but 3 clinical cases were observed at a Phoenix (Ariz.) hospital in the course of 18 months when 7,500 deliveries took place. The 4th case concerned a woman who originally had been treated at another hospital. The 4 cases illustrate 3 types of hydatidiform mole and 3 forms of treatment. In only one of the 3 cases first seen at the hospital was the uterus found larger than the expected gestational size. In the other 2 cases the uterus was believed to be smaller than would be expected. Three of the 4 patients presented themselves with symptoms of bleeding, and only the patient who was first treated elsewhere gave a history of passing the typical grape-like clusters of material. The first case represents a case of syncytial endometritis, which is best treated by repeated curettage and close follow-up. The second case represents the hydropic degeneration of a placenta, with a uterus large enough to require hysterotomy. The third case is that of a true hydatidiform mole, again with a uterus large enough to require hysterotomy. And the fourth case represents a chorioadenoma destruens, with penetration into the uterine wall and requiring hysterectomy for ultimate cure.

Dangers of Oral Therapy of Diabetes During Pregnancy. A. Lass. Geburtsh. u. Frauenh. 18:1167-1171 (Sept.) 1958 (In German) [Stuttgart, Germany].

As the result of careful supervision of the pregnant woman who has diabetes, the mortality of mother and child has decreased, although that of the infant not to the same extent as that of the diabetic mother. Hypoglycemia appears to be one of the chief causes of fetal death. The blood sugar level in the fetal circulation is lower than that in the maternal circulation, and that is why the fetus may die, even though the hypoglycemia in the mother is of a moderate degree. It is an advantage of the oral therapy of diabetes that in patients suited for this treatment hypoglycemic reactions are rare. For this reason it is important to ascertain whether the sulfonylurea compounds, such as carbutamide (BZ 55) or tolbutamide, are suitable for the treatment of diabetes during pregnancy.

The author reports on a 40-year-old pregnant woman in whom diabetes had been observed during the early part of her second pregnancy. After she had been treated with insulin for about 3 months, this treatment was replaced by the oral administration of carbutamide in daily doses of 1.5 Gm. The patient was hospitalized in a precoma state (blood sugar, 390 mg. per 100 cc.) during the 7th month of gestation. No fetal heart sounds were audible. Within a few hours after admission she was delivered of a stillborn child. Chemical investigations revealed a concentration of 1.8 mg. of carbutamide per 100 Gm. in the fetal liver, and this provided clear evidence that the drug had passed through the placenta into the fetal circulation. The woman had taken a total of about 150 Gm. of carbutamide since the third month of pregnancy. Although there is no definite evidence of a causative relationship between the death of the fetus and the presence of the drug in the fetal liver, the possibility of such an interconnection cannot be ruled out. Oral antidiabetic treatment should, therefore, be avoided during pregnancy.

Tuboplasty: Report of 8 Cases with 8 Living Babies. W. R. Knight III. Texas J. Med. 54:728-734 (Oct.) 1958 [Austin].

The author believes that the poor operative results in earlier reports on tuboplasty were mainly due to the inability to control infection and its sequelae, poor materials with which to work, and, above all, poor diagnostic methods with which to select cases. The general clinical examination for proposed tuboplastic procedures should be the same as in any sterility problem. It should begin with taking a complete history and making a general physical examination. Temperature graph, cervical smears, and endometrial biopsy should be obtained for proof of ovulation. Metabolism determinations with either basal metabolic rates or protein-bound iodine determinations should be done, and even minor infractions should be corrected. A sperm count should be performed on the husband. Rubin's test followed by hysterosalpingograms should be done. In most instances the latter is the key to decision as to whether to operate. There must be relative proof that there is no active infection present before a decision is made to perform tuboplasty. The white blood cell count, temperature, and sedimentation rate should be normal.

The histories of 8 women who underwent tuboplasty are presented. Occlusions in most of them were due to infection, but in 2 they were due to salpingitis isthmica nodosa and in 1 to previous operative failure in a congenital defect. Of the 8 patients operated on, 5 subsequently became pregnant, with a total of 8 pregnancies and 8 live births. Only one patient was delivered by cesarean section. There were no ectopic pregnancies or abortions. Four operations were fimbrioplasties, 2 were cornuplasties, 1 was an anastomosis, and 3 were fimbriolyses. Of the latter group, some were done in combination with the other procedures. Tubal patency was demonstrated in all 8 patients. Complications were few. The length of hospitalization averaged 8.6 days. One woman received a blood transfusion, and 7 women received antibiotic therapy for an average of 6 days. In all patients in whom splints were used, the administration of antibiotics was continued postoperatively by mouth for varying periods. Fimbrial occlusion from inflammation was the most common form encountered. This type of occlusion lends itself best to reconstruction and is followed by the highest pregnancy rate.

The Relief of Pain in Spasmodic Dysmenorrhoea by Bromelain. C. A. Simmons. Lancet 2:827-830 (Oct. 18) 1958 [London].

Bromelain, a proteolytic substance extracted from the stem of pineapple fruit, was used over a period of 10 months in 65 female patients. Freeze-dried preparations with the addition of water were employed, and the solution was poured into the vagina and allowed to bathe the cervix. Eighty-nine such treatments were given without complications. In 23 of the 65 patients the drug was given a preliminary trial before surgical intervention or hysterosalpingography. In these patients the clinical effects of the drug occurred within a few minutes of its application; they consisted of softening of the cervix with increased vascularity. The cervical canal, as observed by roentgenography and confirmed by palpation, dilated as far as the internal os. This remained firm except in 2 patients in whom it was physiologically incompetent. Relaxation of the uterine supports may account for the descent of the cervix in some patients. The vagina and cervix were cleared of mucus or discharge by the treatment.

Thirty patients with spasmodic dysmenorrhea received 48 treatments. The results were good on 42 applications; 6 applications failed to give relief, but probable reasons could be suggested for 5 of these failures. Ten patients with congestive dysmenorrhea and 2 with endometriosis received 18 treatments. These patients obtained some relief if a spasmodic element had been present. The optimum time of application was just at the onset of, or shortly before, the period. In some patients relief persisted for as many as 4 cycles after treatment. Ovulation was not inhibited by the treatment. There was no evidence that Bromelain would be of use as an abortifacient; evacuation of the uterus was not made easier by its application. The dramatic effect of the drug on the colicky pain at the onset of the period is due, at least in part, to relaxation of the smooth muscle of the cervix. Perhaps Bromelain affects connective tissue as well as muscle, or possibly the nerves may be affected and may take time to recover.

PEDIATRICS

The Treatment of Newborn Babies Afflicted with Hemolytic Disease Through Sensitization to the Rh Factor. M. Mayer, P. Ducas and A. Sriber. Arch. franç. pédiat. 15:857-895 (No. 7) 1958 (In French) [Paris].

The authors observed 174 babies born to women with the Rh factor who were previously sensitized by a pregnancy or a transfusion. Accidents related to isoimmunization can be prevented by 2 measures: replacement transfusion and concurrent or isolated adrenocortical hormone therapy. Replacement transfusion should be practiced 4 to 6 hours after delivery. Usually the seriousness of the condition of the newborn infant precludes any hesitation about replacement transfusion, but there may be some difficulties in deciding. Symptoms of lesions of the nervous system may be nonspecific and are often the result of anoxia. There is some hesitation when the agglutinin level in the blood is relatively low. There is a parallelism between the number of agglutinins and the degree of fetal impairment. Nineteen deaths are cited, of which 16 occurred in babies whose mothers had titers of irregular antiglobulins of over 1:1,024. Among biological tests indicating replacement transfusion, the best is the bilirubinemia test. There should be an early and continued surveillance of the indirect bilirubinemia level, which should not exceed 20 mg. per 100 cc. Sometimes it is necessary to await this threshold before repeating replacement transfusion. Adrenocortical hormone therapy is used alone or in association with replacement transfusion. Used alone, it should be considered as an exceptional treatment reserved for the newborn infants who are too severely affected to undergo replacement transfusion or for those in whom the condition of erythroblastosis is too minimal to necessitate an immediate decision for replacement transfusion.

Hormone therapy used with replacement transfusion is especially a supportive treatment. It was used in all cases in this series because of the infants' good tolerance of it. A dose of 20 mg. given in 4 administrations was most effective. It is preferred to give adrenocortical hormone therapy immediately after birth rather than after replacement transfusion. Advantages that hormone therapy offer are a better protection against the effects of obstetric shock and consequently a better tolerance to replacement transfusion, a shortening (not constant) of the period necessary for the disappearance of icterus and the return of the level of bilirubinemia to its normal figure, a more rapid absorption of edema, a more constant regularization of the weight curve, and the disappearance of the Coombs sign. Cortisone and its derivatives have a debatable influence on hematopoiesis and on the prevention of lesions of the nervous system. Study of more series is necessary.

The authors prefer to interrupt pregnancy when dangers of sensitization are clearly present and particularly when there are complications of pregnancy. Interruption avoids the last 6 weeks of pregnancy, the period which brings the most risks to the fetus. Premature babies are less afflicted with erythroblastosis than babies who have reached term and who have suffered from prenatal anoxia. Anoxia and obstetric shock have serious consequences which may be combatted with digitalis treatment and neuroplegics. The majority of deaths occurring on the first day are the result of cardiac insufficiency. The authors treated secondary infections with combinations of penicillin and streptomycin or ganidan. Babies in this series were given liver extract, methionine, and vitamin B^{12} for protection against hepatic lesions. None of them had abnormal prolongation of icterus or bile retention or any indication of cirrhosis.

There were 11 deaths (7.3%) among 150 babies born in the maternity department of Saint Antoine Hospital, Paris. They occurred in babies severely affected with lesions of the nervous and pulmonary systems. Twenty-four babies were brought to Saint Antoine from other maternity centers. The majority of them arrived in very poor general condition, and 11 died relatively soon after their admission. This large percentage of deaths was probably due to the delay in replacement transfusion. Long-range results of treatment are encouraging and include complete disappearance of signs of kernicterus and blood disease.

Immediate Results of Replacement Transfusion in the Treatment of Hemolytic Disease of the Newborn. T. Boreau and G. David. Semaine hôp. Paris 34:2182-2185 (Aug.-Sept.) 1958 (In French) [Paris].

During the first 8 months of 1957, 186 infants were given 265 replacement transfusions at the Center for Blood Transfusion in Paris. The authors analyze the results, stating that their only modification of the technique consisted in practicing transfusion under neuroplegics. During the intervention Largactil was administered in an average dose of 1.5 mg. per kilogram in 5 injections. After the intervention it was administered by mouth 3 times in an average dose of 1 mg. per kilogram during 3 hours. Since the danger zone of bilirubinemia is considered to be 18 to 20 mg. per 100 cc., replacement transfusion was practiced as soon as possible after birth in babies with clinical signs of hemolysis. Indications for replacement transfusion were much rarer in those with hemolytic disease of the newborn in whom there was incompatibility of the 3 blood groups, O, A, and B, than in those with incompatibility of the Rh factor.

Immediate results of the replacement transfusion treatment were observed during the first 10 days of life. These pertained to mortality, to changes in icterus and level of bilirubin, and to disorders of the nervous system. No deaths occurred during the exchange among the 186 infants given replacement transfusions. The 3 types of complications arising during the operation have common signs; these types are hypocalcemia, which is proved by response to injection of calcium; blood overloading, which is distinguished by the rales of pulmonary edema; and excessive withdrawal of blood, which is corrected by restoring the quantity of missing blood, usually 10 to 20 cc. There were no deaths among infants with hemolytic disease from OAB incompatibility, but there was a mortality rate of 3.1% among those with hemolytic disease from Rh incompatibility. Delay in transfusion of 12 hours or more resulted in 2 deaths among the 53 infants treated after such a delay. Among infants who received replacement transfusions early, death occurred in none of the 37 who had reached term at delivery, in 1 of the 23 who were spontaneously premature, and in 2 of the 47 who were born by induced delivery. This disease progresses rapidly, and results of replacement transfusion were quickly compromised when the exchange was not performed early. The possibility of serious affliction in utero justifies interruption of pregnancy in spite of a slight increase in postnatal risks. In this series prenatal mortality usually reached 20% among those with hemolytic disease, but it fell to 10% with the practice of induced delivery.

It is rare that icterus increases to the point of necessitating additional replacement transfusion in OAB-type hemolytic disease, but in this series 36% of the infants with Rh-type hemolytic disease required it. Risk of complications in the nervous system is much greater in hemolytic disease from Rh incompatibility. Signs of abnormality increased when transfusion was delayed. Ten per cent of the infants treated after the 12th hour presented signs of disorders of the nervous system. The only infants without signs were those delivered at term. A significant number of premature infants (5%) presented signs. It is impossible to evaluate the importance of these signs without the passage of more time, but they have generally been interpreted too quickly as indicative of kernicterus.

Chediak's Anomaly of Leukocytes in Malignant Lymphoma Associated with Leukemic Manifestations: Case Report with Necropsy. P. Efrati and W. Jonas. Blood 13:1063-1073 (Nov.) 1958 [New York].

The authors report the occurrence of Chediak's anomaly of leukocytes in an 11-month-old boy with leukemic manifestations, who was admitted to the pediatric department of the Kaplan Hospital in Rehovoth, Israel, because of a febrile disease of 5 days' duration. On admission he was severely ill;

his temperature was 104 F (40 C). Laboratory studies revealed a greatly increased number of leukocytes with immature and abnormal cells in the peripheral blood, anemia, and thrombocytopenia. There was enlargement of the spleen, liver, and lymph nodes. The infant was not an albino, and no pathological changes were noted in the skin. The parents were not related, and a second infant, a girl, was healthy. The patient was treated with daily injections of 600,000 units of penicillin and 40 mg. of corticotropin (ACTH), a transfusion of 150 cc. of whole blood, and infusions of sodium chloride solution and dextrose. The patient's condition remained critical, and 5 days after admission he died with signs of anoxia. Autopsy revealed a malignant lymphoma of the lymph nodes with diffuse infiltration of all the internal organs.

This case is the 4th of Chediak's anomaly reported in the literature. All 4 cases had in common enlargement of the spleen, liver, and lymph nodes and characteristic changes in the leukocytes—Doehle bodies in the neutrophils and inclusion bodies in the mononuclears. In this patient, in addition to the giant eosinophilic granules in mature eosinophils described by Chediak, peculiar large mononuclear cells, often very young, were found; some of them contained inclusion bodies. These cells were believed to be malignant lymphoma cells that found their way into the blood stream. It is difficult to decide whether Chediak's anomaly is a hereditary entity; the consanguinity of the parents in 2 of the 3 cases collected from the literature and the abnormality in the leukocytes of other members of the family seem to strengthen this hypothesis. The other possibility is that one is dealing with a degenerative phenomenon in the leukocytes due to a systemic disease. The authors consider it possible that in all the reported cases there were generalized pathological changes in the reticulohistiocytary system.

Prognosis in Legg-Perthes Disease. H. M. Broder. J. Pediat. 53:451-463 (Oct.) 1958 [St. Louis].

The author studied the records of 208 patients with osteochondrosis of the capital epiphysis of the femur (Legg-Calvé-Perthes disease) in order to determine factors of prognostic significance. The age of the patient, the severity of involvement, and the status of progression of the disease when treatment was begun were found to exert a direct influence on the end-result. The younger patient with less severe involvement treated early in the disease has an excellent prognosis. The prognosis becomes less favorable with more severe involvement or when treatment is not started until later in the disease process. Since complete bed rest with or without traction achieves no better results than the ambulatory non-weight-bearing methods, the latter are preferable except in cases of bilateral simultaneous involvement. Earlier studies had shown that ultimate degenerative changes and disability are directly related to the severity of deformity caused by this disease. Only patients with hips in which excellent results were obtained may be expected to go through life without further difficulty from this source.

The Bacteriological Diagnosis of Childhood Tuberculosis Using Bone Marrow and Peripheral Blood Aspirates. L. S. Kimsey. J. Pediat. 53:413-431 (Oct.) 1958 [St. Louis].

The 30 patients in whom the author resorted to the use of bone marrow and peripheral blood aspirates in the bacteriological diagnosis of childhood tuberculosis are divided into 3 groups. The 13 children of the first group had tuberculosis that was uncomplicated by meningitis. Smears of the concentrated bone marrow were positive for acid-fast bacilli in 5 of the 13 patients, and 2 of the 5 specimens were positive for Mycobacterium tuberculosis by both cultural methods and animal inoculation. Smears of the concentrated blood were positive for acid-fast rods in 7 of the 13 patients, and Myco. tuberculosis was isolated from 2 of the 7 patients with positive blood smears. Series 2 was composed of 11 children who had a final diagnosis of tuberculous meningitis. Smears of the concentrated bone marrow specimens were positive for acid-fast rods in 8 of the 11 patients of this group, and 5 of the 8 were positive for Myco. tuberculosis by both cultural methods and animal inoculation. Smears of the concentrated blood were positive for acid-fast rods in 5 of the 8 patients for whom the bone marrow smears were positive, but Myco. tuberculosis was not isolated from the blood specimens. The 6 children of the third series served as controls, since they were nontuberculous. Acid-fast bacilli were not seen in the clinical specimens, nor were they isolated by either culture or animal inoculation.

To illustrate the usefulness of bone Marrow and blood aspirates in the diagnosis of tuberculosis in children, the case histories of 3 patients were reviewed. The final diagnoses of the cases selected were miliary tuberculosis, tuberculous peritonitis, and tuberculous meningitis. Although the number of clinical cases is limited, the results of this investigation indicate that bone marrow and blood aspirates are useful in establishing the diagnosis of tuberculosis in children. These methods are not offered as substitutes for the usual laboratory procedures, but they provide additional sources of information if the study of the routine specimens proves unrewarding. The methods are especially valuable in tuberculous meningitis and miliary tuberculosis where the patient's life is dependent upon the early recognition and treatment of the disease.

Treatment of Recurrent Convulsions in Children. H. M. Keith. Journal-Lancet 78:461-464 (Nov.) 1958 [Minneapolis].

A review of the literature on the treatment of recurrent convulsions in children revealed that convulsive attacks were arrested by the administration of bromides in 23.5% of 366 patients, and remissions ranging from 6 months to 10 years were produced by the use of triple bromides or phenobarbital or by the combined administration of the two drugs in 61% of 543 patients. Convulsive attacks were controlled or decreased for up to 5½ years with the use of diphenylhydantoin (Dilantin) sodium and phenobarbital in 79% of 319 patients. The author treated 190 children with grand mal or petit mal seizures or both types of seizures by placing the patients on a ketogenic diet, which was calculated for the individual patient as follows: The number of calories allowed was 55 per kilogram or 25 per pound of body weight. The amount of protein was set at 1 Gm. per kilogram of body weight, which was found to be satisfactory. The carbohydrate and the fat were then adjusted, so that the ratio of the ketogenic to the antiketogenic material was at least 3 to 1. When the diet was begun, the amount of carbohydrate taken was decreased and the amount of fat was increased over a period of 4 days. This gradual change almost always prevented nausea and vomiting, which might have occurred had the children been given the full diet immediately. Of the 190 children, 35.3% remained entirely free of attacks for 4 to 22 years, although treatment actually lasted only 1 to 3 years, and another 8.4% improved.

From these data it seems encouraging that complete control of convulsive attacks can be obtained in 23.5% to 35.3% of patients for as long as 22 years, and the seizures of many more patients are completely controlled for shorter periods. Surgical treatment may control attacks in 56% of specially selected cases. In addition, many patients may be greatly helped by these forms of treatment, although their convulsive attacks may not be entirely eliminated.

Hyperbilirubinemia in the Premature. S. Dundon. J. Irish M. A. 43:281-287 (Oct.) 1958 [Dublin].

The author reports on 58 premature infants (whose birth weight was 2,640 Gm. [5½ lb.] or less), born at the National Maternity Hospital in Dublin, whose bilirubin levels were of such degree as to require exchange transfusions. One hundred thirty-four exchange transfusions were carried out on these infants. Forty of the 58 infants had hemolytic disease of the newborn; these infants received 111 exchange transfusions, and there were 2 deaths in this group, one from cardiac failure and the other from intracranial hemorrhage. The remaining 18 infants, who received 23 exchange transfusions, had hyperbilirubinemia unassociated with any blood incompatibility; there were no deaths in this group. No cases of kernicterus were found in either group. It is almost certain that kernicterus will not develop in any infant if the serum bilirubin is maintained below a level of 20 mg. per 100 cc. The importance of early recognition of jaundice and subsequent regular bilirubin estimations is stressed.

Multiple exchange transfusions are simple and of great value. No premature infant with hyperbilirubinemia associated with hemolytic disease should receive an exchange transfusion unless for some definite reason, such as cardiac failure, rapidly developing hemolysis, or danger level of bilirubin. Whereas death might occur from cardiac failure, no death should result from the procedure of exchange transfusion. Repeat exchange transfusions should be carried out to maintain the bilirubin level below 20 to 25 mg. per 100 cc. Although the cause of hyperbilirubinemia in the premature infant without hemolytic disease is unknown, the treatment should be again merely one of exchange transfusion to keep the bilirubin level below 20 to 25 mg. per 100 cc. Regular bilirubin estimation by a reliable method is essential. An association between asphyxia, edema, and jaundice was noted in the premature infants with hyperbilirubinemia unassociated with hemolytic disease; a similar association with maternal diabetes and jaundice in the newborn infant also was observed in this group of premature infants.

Education of Cerebral Palsied Children: The Role of Meprobamate: A Preliminary Evaluation. B. E. Katz. J. Pediat. 53:467-475 (Oct.) 1958 [St. Louis].

The education of children with cerebral palsy must include some means of reduction of spastic or involuntary movements. The intent of this study was to ascertain whether meprobamate could influence the ability of children with cerebral palsy to learn. In the cerebral palsy school of Twin Falls, Idaho, enrollment is restricted to handicapped children with symptoms referrable to brain lesions. The local board of education furnishes 2 teachers and school supplies. Parents and local service groups support the project's therapeutic needs, including the services twice weekly of a physical therapist, but the school is primarily for instruction. Of 19 patients enrolled, 10 with cerebral palsy were selected for this study. All 10 patients, who ranged in age from 5 to 24 years, had received instruction and undergone evaluation for at least

2 years prior to the study. All 10 could sit upright for varying periods, although 3 required mechanical support. Two patients were confined to wheel chairs, but the others were ambulatory.

The 80-week study began in September, 1956. Base-line responses were established in the first 6 weeks and compared with those noted in prior years. Meprobamate was given to the 10 patients by an instructor once daily and was swallowed in her presence. The treatment was begun with small doses. If there was no response after 2 weeks' medication, dosage was increased until a response was obtained. Blood studies and urinalysis were performed after maximum dosage was reached, and once thereafter. Medication was suspended over the summer vacation (i. e., after 35 weeks' observation) in all but 3 cases. Administration of meprobamate was resumed in the fall, during the 52nd week of the study. The following factors were evaluated at weekly intervals: degree of muscle relaxation, magnitude of spastic or involuntary movement, ease of handling, outlook and attitude, endurance, attention span, and ability to learn. Nine of the 10 patients under therapy completed the school year with increased attention span and improved ability to learn. Scholastic progress among these 9 was beyond that anticipated from earlier observation. Since the 9 children at the school who received no meprobamate continued to progress at the same retarded rate observed previously, the author concludes that in selected patients with cerebral palsy meprobamate can encourage scholastic performance at maximum capacity and can improve response to instruction.

Acquired Primary and Idiopathic Anemia in the Younger Infant. M. Berkman. Semaine hôp. Paris 34:2186-2195 (Aug.-Sept.) 1958 (In French) [Paris].

The author, from 200 observations of primary anemia published since 1925, considers 63 cases occurring between birth and 4 years of age, of which 35 began in babies not more than one year old. The fundamental distinction between congenital and acquired anemia should be maintained. The forms of anemia may be with or without icterus, hemoglobinuria, and detectable antibodies. During childhood acquired primary and idiopathic anemias are rare but not exceptional, and affect selectively the youngest age group. The clinical picture shows a sudden intense anemia associated with severe disturbances in the general condition. The tendency toward regeneration (blood reticulocytosis, medulla erythroblastosis) is generally obvious. Increased elimination of fecal stercobilinogen constitutes the best biological criterion for affirming hemolysis, but it is often difficult to appraise in the infant. The immunological studies are particularly interesting, but the results are inconsistently reliable. Hemolysins are detected with increasing frequency. In the newborn infant hemolytic anemia from autoantibodies is exceptionally encountered.

The forms of anemia with erythroblastopenia, absence of regeneration, and often with association of thrombopenia and of granulopenia have poor prognosis, but this has been notably improved by the use of corticotherapy. Likewise, hormone therapy has improved the prognosis for chronic forms, which are rare but possible in the young child and which develop by successive acute exacerbations. Treatment is based on blood transfusions, splenectomy, and corticotherapy. Transfusions carried out for mere substitutive purpose can in certain cases provoke aggravations which may be due to the introduction of the serum complement indispensable for the action of immune hemolysins. Splenectomy is now replaced by corticotherapy, which revolutionized the treatment of severe forms. The author holds that acute hemolytic anemia (Lederer-Brill disease) has no proper autonomy. It is a syndrome, which in its idiopathic form often seems to have been launched at an early age by the intervention of autoantibodies and especially of serum hemolysins.

Undescended Testis. M. LeLong, P. Petit, P. Canlorbe and others. Semaine hôp. Paris 34:2487-2495 (Oct. 24) 1958 (In French) [Paris].

The authors conducted systematic research at the auxoendocrinologic center of the Saint Vincent de Paul Hospital in Paris on undescended testes. The subjects were 32 boys, 20 with unilateral ectopia and 12 with bilateral ectopia, on whom 28 biopsies were performed. It is indispensable to use histological studies of specimens from biopsies done at the time of intervention and repeated several years later, if necessary, in order to evaluate fertility. The risks of sterility are greater in proportion to the lateness of descent of the testes. Descent before the age of 10 years does not guarantee against infertility, even when the ectopia is unilateral. Sterility risks are particularly great in bilateral undescended testis, but these risks exist also in unilateral undescended testis where the spontaneously descended testis may be functionally insufficient.

In this series the testicular anomaly did not cause any modification of the morphologic development, of bone maturation, or of urinary elimination of 17-ketosteroids. In the 14 children with one undescended testis who were operated on at 10 years of age or later, the testis was of a volume inferior to the normal volume for the age in 10 cases. It was normal in only 4 cases. In the group of 12 bilateral ectopias the 2 testes appeared normal in only one case. In both groups of the series, fibrous lesions of the canal or around the testis necessitating dissection were present in 11 cases. Among the 28 biopsies, only 2 indicated normal testes, and these were in children who had been operated on at 5 years of age. In the remaining 26 cases there were severe lesions. The earliest lesions affect the insterstitial tissue and can already be seen in 6-year-old boys. Fibrosis is at first perivascular; peritubular fibrosis seems to appear after the 8th year. From the 7th year the seminiferous tubules are clearly less developed than those of normal children of the same age. Biopsy of the testis which appeared morphologically the most normal in a 28-year-old man who had orchiopexy at age 12 indicated lesions, sclerosis, and total absence of spermatogenesis.

These clinical and histological findings have dictated a specific line of conduct systematically applied to every child sent to the center for undescended testis. This includes studies of familial antecedents, personal history (scrotal hematoma or inguinal hernia), bone maturation, and hormones. There is also a clinical examination, including a morphologic study, a study of sexual development, and an examination of the testes. Surgical intervention is the treatment of choice. Orchiopexy is only legitimate if it is performed early (age 5 or 6 years) and carefully. Results cannot be precisely determined until 2 months have passed. Hormone treatment alone has no results, but it can be valuable as postoperative therapy and may influence the regression of lesions. Surgical intervention should be in 3 phases: (1) search for anatomic cause; (2) lowering of testis; and (3) fixation. The future functioning of an undescended testis is difficult to appraise. After the first year the chances for spontaneous descent are much lessened.

Late Results of Treatment of Testis Retention. H. Hamelmann. München. med. Wchnschr. **100:** 1559-1561 (Oct. 10) 1958 (In German) [Munich, Germany].

The author stresses that improvement in cosmetic appearance is not an adequate criterion in the evaluation of the results of treatment of undescended testes. The important factor is evidence of fertility. When such evidence is missing, the efficacy of conservative or of surgical therapy cannot be definitely evaluated. Follow-up examinations based on the evidence of fertility showed unexpectedly poor results after spontaneous descent and after operative correction in cases of unilateral as well as of bilateral testis retention. Based on the experience that the dystopic testis is subjected to an increasing inhibition of development from the 5th year of life onwards, operative transposition of the testis should be done at an earlier time than has hitherto been customary. The most favorable moment for operative transposition is between the 5th and the 6th year of life. How far the later results can thereby be improved remains to be seen.

UROLOGY

The Technique of Renal Biopsy Used at Hôpital Necker. J. Hamburger. Presse méd. **66:**1451 (Sept. 24) 1958 (In French) [Paris].

The deficiencies and dangers of both transcutaneous needle biopsy of the kidney and the standard surgical biopsy led the author to use a combination of these methods in which a needle biopsy is carried out under visual control by way of a slight surgical operation providing access to the external edge of the kidney. A small external oblique incision, carried downward and forward, is made below the costal margin, with the patient in lateral decubitus under general anesthesia. This approach, because it keeps the procedure retroperitoneal and makes it unnecessary to traverse the thick lumbar muscles, causes very little trauma. A Brun-Iversen needle, fitted with a small adjustable slide by which the degree of penetration into the kidney can be fixed in advance, is then inserted through an incision of a few millimeters in the renal cortex; the special syringe is attached to the needle, and a delicate cylindrical specimen of renal tissue is obtained by aspiration. Care must be taken to see that the tiny renal wound is not bleeding before the entrance wound is closed; if any oozing of blood is observed, a little thrombin can easily be applied. A suture in the renal capsule is a further safeguard against delayed bleeding. Closure of the superficial planes then follows.

This method, which is not subject to the failures that often accompany transcutaneous puncture and which is less hazardous and traumatizing than the standard surgical biopsy, has been used in 110 patients without complications of any kind. Hematuria, even of a microscopic character, was often not evident in these patients the day after the operation. The method, however, is contraindicated in patients with hemorrhagic conditions or far-advanced renal insufficiency.

Internal Diameter of Renal Artery and Renal Function. N. S. R. Maluf. Surg. Gynec. & Obst. **107:**415-428 (Oct.) 1958 [Chicago].

Performance of a few hundred aortograms, while on the urologic service of 3 institutions, and study of the respective patients impressed the author with the fact that there tends to be an association between the caliber of the renal artery or arteries and the magnitude of renal function. The author analyzes this impression with the aid of translumbar aortography. He found that the internal diameter of the renal artery of a young human adult with 2 normal kidneys is 6.6 mm. When a kidney receives more than one artery from the aorta, the equivalent diameter can be computed from an equation which is formulated by the author. The internal diameter of the renal artery of a hypertrophied solitary kidney is about 8.5 mm. The increase in diameter over that of the artery to a kidney of a normal pair is quite adequate to accommodate the doubling in blood flow through the hypertrophied kidney without necessitating any changes of pressure-head or of peripheral resistance. The ratio of internal diameter of renal artery to splenic or hepatic artery is typically greater than unity when the kidney is normal. The ratio rises in renal hypertrophy and falls in renal hypoplasia or reduced renal function.

The internal diameter of the renal artery of the congenital polycystic kidney was found to be remarkably narrow. The internal diameter of the renal artery in advanced hydronephrosis was as follows: (*a*) normal in advanced hydronephrosis from acute ureteral obstruction; (*b*) normal in intermittent hydronephrosis when renal function was not markedly reduced; (*c*) markedly narrowed in prolonged hydronephrosis with consequent renal atrophy. Narrowing of the internal diameter of the renal artery in cases of prolonged hydronephrosis is the result of enlargement of the intima by cellular proliferation and fiber deposition. A narrow renal artery is always indicative of reduced renal function, but an artery of normal caliber (by aortography) does not necessarily imply normal renal function. Assistance in renal evaluation should be obtained from the intensity of the instantaneous nephrogram. Kidneys with large "solitary" cysts characteristically do not have a narrower renal artery than the contralateral normal kidney.

Urologic Pitfalls in the Management of Carcinoma of the Cervix. C. J. E. Kickham. J. Urol. 80:229-236 (Oct.) 1958 [Baltimore].

On the basis of extensive experience in the care of urologic problems of carcinoma of the cervix and an opportunity to evaluate approximately 1,700 victims of this disease from the urologic viewpoint, both before and after treatment, the author is convinced that, except in well-organized clinics, the services of the urologist are requested in most instances only when the gynecologist is faced with a perplexing problem. It becomes, therefore, the responsibility of urologists to instruct the medical student, the house officers, the practicing physician, and the gynecologist, in particular, concerning the tragedies which may follow on the heels of failure to recognize and adequately manage the urinary tract in patients with carcinoma of the cervix. Complications that involve the bladder and ureter may be the result of the natural progress of the disease or an effect of treatment. Neurogenic vesical dysfunction and damage to the ureter are frequent sequelae of radical hysterectomy and lymphadenectomy carried out for the removal of cervical carcinoma. Methods of urinary diversion are described in relation to ureteral involvement or damage in carcinoma of the cervix.

The value of nephrostomy is particularly stressed. It is an operation devoid of shock, with practically no mortality, and affords ideal drainage. There should be no hesitancy to perform it as a temporary or even permanent means of urinary diversion in the presence of a ureterovaginal fistula or ureteral obstruction. The future of the severely obstructed and severely infected kidney may be better served by prompt drainage through nephrostomy, which may serve as a protective mechanism for exploration and repair of the ureter later. The role of ultraradical surgery in advanced cervical malignancy is discussed and its contraindications stated. The sacrifice of a kidney is not too high a price to pay for cure in this group of patients. The problems encountered in both radical and ultraradical surgery attest to the prime necessity of the urologist and gynecologist being proficient in the surgical disciplines of each others' fields as well as being familiar with the technical fundamentals of intestinal surgery. This is a requisite for the proper management and best interests of victims of cancer of the cervix.

Contemporary Indications for Partial Nephrectomy in Patients with Tuberculosis. S. Petković. Urol. internat. 6:155-167 (No. 3) 1958 (In German) [Basel, Switzerland].

The author reports on 710 patients with tuberculosis of the kidney who were treated at the urologic clinic of the University in Belgrade, Yugoslavia, between 1950 and 1957. Of the 710 patients, 412 (59%) received chemotherapy, 275 (38%) underwent total nephrectomy, and 14 (2%) were subjected to partial nephrectomy, while 9 (1%) refused treatment. None of the 14 patients undergoing partial nephrectomy died. Rather limited indications for total nephrectomy still persist, but it is no longer considered an operation which must be performed immediately. Total nephrectomy is the method of choice for patients with chronic destructive forms of unilateral or even bilateral renal tuberculosis, provided that the changes in the other kidney promise healing of the lesions with the aid of antibiotics or partial nephrectomy. Advanced changes in the renal tubules, considerable destruction in the kidneys, and the age of the patient remain the basic indications for total nephrectomy. The indications for treatment with tuberculostatic agents have been widened. The presence of cavities of recent origin is no longer a contraindication, provided that the condition of the tubules is satisfactory. Ulcerated, even dispersed lesions, if they show a tendency toward healing with the aid of antibiotics, are no longer indications for nephrectomy. Moderate lesions of the tubules, stenosis of the pelvic portion of the ureter which does not progress, and stenosis of the lower portion of the ureter which is not advanced no longer require nephrectomy, at least before a chemotherapeutic trial.

The indications for partial nephrectomy lie midway between those for total nephrectomy and chemotherapy. At the start of the antibiotic era they were widened at the expense of total nephrectomy, and at present they become more limited at the expense of chemotherapy, since many patients may be given combined treatment with various antibiotics for prolonged periods ranging from 2 to 5 years. Right now, the best indications for partial nephrectomy are isolated cavities with old rigid walls, which suppurate continuously and are associated with persistence of Mycobacterium tuberculosis in the urine for prolonged periods. Treatment of ulcerative lesions in an early stage and small cavities of relatively recent origin should be given a trial with tuberculostatic agents.

INDUSTRIAL MEDICINE

Disability and Mortality from Chronic Bronchitis in Relation to Dust Exposure. C. M. Fletscher. A. M. A. Arch. Indust. Health 18:368-373 (Nov.) 1958 [Chicago].

According to the author, chronic bronchitis, a condition characterized by persistent or recurrent cough and expectoration, which is not due to localized bronchopulmonary disease and which is often associated with exertional dyspnea, is an important cause of morbidity and mortality in the working classes in Great Britain. While men who work in dusty occupations, especially coal miners, have a higher prevalence of the symptoms of bronchitis and emphysema, with respiratory disability, than control groups of men, there is no close relationship between the duration of such exposure and the prevalence. There are 2 possible explanations for this apparently contradictory finding: 1. Dust exposure is not the factor responsible for the increase of bronchitis in miners and foundry workers, such as revealed by British official mortality figures, but it is some other contrasting environmental factor, such as temperature changes on leaving work, heavy exertion, or exposure to some unidentified irritant. 2. Dust exposure is responsible, but the relationship between the severity or duration of such exposure and the onset of bronchitis is not a simple quantitative one.

The important fact remains that there is at present some evidence that workers in dusty industries, such as coal mining and foundry working, have an undue prevalence of respiratory symptoms and of impaired ventilatory capacity resulting in respiratory disability. There is also evidence that, at least in Great Britain, an excessive number of deaths from bronchitis and emphysema occur in men who are exposed to the smoky atmosphere of the cities and who indulge in the habit of cigarette smoking. Surveys of respiratory morbidity in workers exposed to respiratory irritants and in control groups in Great Britain and in the United States, where bronchitis may be less prevalent, could help to elucidate this important problem to industrial health.

Basal Cell Epithelioma Following a Single Trauma. M. Reisch. Indust. Med. 27:533-534 (Oct.) 1958 [Chicago].

A 49-year-old man struck his forehead on a show case, sustaining a laceration about 2 cm. in length. Bleeding subsided under pressure dressings. Since there was no indication of healing after 10 days, the man consulted his physician who prescribed an ointment. The patient applied the ointment for about 3 months, and the wound finally healed. Three days later a small ulcer appeared, which gradually enlarged. Seven months after the injury there was an oval eroded lesion. Biopsy revealed a disseminated basal-cell epithelioma. The lesion was removed by electrodesiccation and curettage, followed by the application of a solution of acid nitrate of mercury (Sherwell method). The wound healed within a brief period, leaving a soft, pliable, slightly depressed scar.

According to the patient, the injured area was "normal" before the accident. Examination of the face showed no indication of any keratoses, freckling, adenomas, scars, or other pathological lesions. He had never previously had an epithelioma or radiation therapy, nor did he have the complexion of one predisposed to epithelioma. The history indicates that a basal-cell epithelioma developed within the area of an unhealed, incised wound after a sharp blow to the skin. The lesion was clinically manifest probably 3 months after the injury.

It is difficult to establish whether a single mechanical injury to the skin is the sole precipitating cause of epithelioma. The principal problem is that there never is assurance that the injured area was previously normal. Then, one must consider that statistics covering traumatic injuries show the incidence of malignant epithelial neoplasms to be extremely low (37 epitheliomas in 26,000 cutaneous injuries).

THERAPEUTICS

The Status of Phenylbutazone (Butazolidin) in the Treatment of Rheumatic Disorders. W. Graham. Canad. M. A. J. 79:634-638 (Oct. 15) 1958 [Toronto].

Phenylbutazone was given to 270 patients, 24 of whom had gouty arthritis, 23 had ankylosing spondylitis (Strümpell-Marie disease), 58 had osteoarthritis, 86 had rheumatoid arthritis, and 79 had miscellaneous conditions, such as disk syndrome, tendinitis, and bursitis. A dosage schedule of 600 mg. daily for 2 days, 400 mg. for 2 or 3 days, and then a maintenance dose of 100 to 300 mg. daily was used. A daily maintenance dose of 200 mg. was usually sufficient to maintain a constant therapeutic blood level, and 100 mg. daily was sufficient in a few patients with spondylitis. Eight patients with duodenal ulcer and one who had been operated on for carcinoma of the stomach received phenylbutazone in the form of suppositories, each containing 250 mg. The result from suppositories was equal to that from oral administration.

Results showed that, if additional medication other than less toxic salicylate compounds is found to be necessary, phenylbutazone is the drug of choice in the treatment of ankylosing spondylitis. In gouty arthritis, phenylbutazone is at least equal to, and in some reports better than, colchicine given orally, with less gastrointestinal disturbances. In patients with rheumatoid arthritis, rheumatoid arthritis associated with psoriasis, osteoarthritis, disk lesions, and some other miscellaneous rheumatic disorders, a trial of phenylbutazone should be considered; administration of the drug should be discontinued if no relief is obtained in one week. In postherpetic neuralgia the results obtained with phenylbutazone appeared to be superior to those with previous forms of therapy, but a larger study is required.

Most of the complications of phenylbutazone therapy were minor and transient in nature. Major reactions occurred in 6 patients (2.2%), 2 of whom had pulmonary edema, 1 had hemorrhage from a duodenal ulcer, 1 had severe dermatitis, 1 had severe vomiting, and 1 had hepatitis; none of these major reactions was fatal, and all subsided on cessation of therapy. The danger of toxicity is reduced by close clinical observation of the patient and prompt withdrawal of the drug at the first sign of an undesirable reaction. Administration of phenylbutazone should be avoided in patients with a history of peptic ulcer, hypersensitivity, or congestive heart failure. The lowest possible maintenance dose should be used, and administration of the drug should be discontinued if no improvement is noted in 7 days. In this series of patients, blood studies revealed no toxic effect of the drug on blood or bone marrow.

Increased Resistance to Antibiotics Among Micro-organisms Isolated in a General Hospital (1956-1957). A. J. Weil. New York J. Med. 58:3102-3108 (Oct. 1) 1958 [New York].

The micro-organisms isolated from clinical specimens in the Bronx Hospital, New York, have been tested for sensitivity to antibiotics since 1950, and the results of these tests have been subjected to repeated surveys. The experience in this hospital reflects the general trend of emerging resistance to antibiotics as a result of the aggressive use of these agents. This paper presents the data from antibiotic sensitivity tests on 1,387 strains of bacteria isolated from medical and surgical specimens in 1956-1957 and compares them with those from 1,117 strains collected in 1953-1954. The micro-organisms belonged to the following groups: streptococci, staphylococci, Escherichia and Proteus organisms, Aerobacter aerogens, Pseudomonas aeruginosa, and Alcaligenes fecalis. They were tested for sensitivity to penicillin, erythromycin, tetracycline, chloramphenicol, streptomycin, and polymyxin B.

A significantly higher incidence of resistance to a variety of commonly used antibiotics was observed in 1956-1957 than in 1953-1954. The increased frequency in resistance to tetracycline was particularly impressive. Staphylococci, particularly those that were mannitol and coagulase-positive, and A. aerogenes frequently showed resistance to a variety of antibiotics. These organisms also became more prevalent. The incidence of staphylococci and of A. aerogenes increased from 13.1 and 11.7% of all isolations in 1953-1954 to 20.8 and 19.3%, respectively, in 1956-1957. The ability to produce resistant mutants gives these 2 groups of micro-organisms a competitive advantage under conditions in which antibiotic therapy is widely used. In view of the frequency with which resistance was encountered to the 6 antibiotics used previously, the routine of testing was extended to neomycin, novobiocin, and, for urinary cultures, nitrofurantoin. Very few strains were encountered that were resistant to every one of the agents tested. Under the conditions of high incidence of resistance, infections from which 2 or more different bacteria are isolated sometimes pose a problem in finding a single agent inhibiting all the micro-organisms found in a given disease. Neomycin and chloramphenicol offered the widest coverage of multiple infections.

Surgical Collapse During and After Corticosteroid Therapy. R. I. S. Bayliss. Brit. M. J. 2:935-936 (Oct. 18) 1958 [London].

Corticosteroid therapy, especially if prolonged, causes adrenal suppression. Surgical procedures increase the need for adrenocortical secretions, and may lead to fatal collapse in patients who are currently receiving steroid therapy or have had such treatment within the previous 2 years. To prevent disasters, such as irreversible fatal shock occurring in a 34-year-old man with rheumatoid arthritis, who had a cup arthroplasty performed on his hip after having been treated with cortisone for the previous 18 months (The Journal 149:1542 [Aug. 23] 1952), it is essential to know before operation whether the patient is having or has had steroid therapy. Patients currently having steroid treatment need more, not less, corticosteroid during the operative period. They and those who have had steroid treatment during the previous 18 months should be given 100 to 200 mg. of cortisone acetate by the intramuscular route 24 hours and again 4 hours preoperatively. Postoperatively, 100 to 200 mg. of cortisone should be given daily and should gradually be reduced over a period of one week; administration should be by mouth if the patient is not vomiting and by the intramuscular route if he is. It is usually safe to omit special preoperative measures in patients who have stopped steroid therapy more than 18 months previously, provided that a careful watch is kept on the pulse and blood pressure and that, if collapse occurs, immediate treatment is available with hydrocortisone sodium succinate, which should be given by the intravenous route in doses of 100 to 400 mg. per 24 hours.

Antituberculous Activity of Thiocarbanidin in Vitro and in the Experimental Animal. W. Steenken Jr., V. Montalbine, M. M. Smith and E. Wolinsky. Am. Rev. Tuberc. 78:570-575 (Oct.) 1958 [New York].

Thiocarbanidin is chemically described as 4-isobutoxy-4′-(2-pyridyl) thiocarbanilide and has been shown to be active against human tubercle bacilli in vitro and in the laboratory animal. This paper reports on further studies with this drug. Liquid Tween-albumin medium was used to test the in vitro activity of thiocarbanidin against the following strains: (1) H37Rv, (2) H37Rv resistant to thiosemicarbazone, aminosalicylic acid, and isoniazid, (3) 4 recently isolated strains of tubercle bacilli, and (4) 4 atypical photochromogenic strains of mycobacteria. A stock solution of the drug was prepared to contain 40 mg. per milliter in dimethylacetamide from which serial dilutions in mediums were made. The inoculum into each tube was 0.1 ml. of a 10-day culture of micro-organisms in Tween-albumin medium.

Thiocarbanidin inhibited the in vitro growth of H37Rv, of H37Rv resistant to isoniazid and aminosalicylic acid, and of 4 freshly isolated strains of tubercle bacilli. The drug also inhibited the growth of 4 photochromogenic strains. An H37Rv thiosemicarbazone-resistant strain grew in the presence of thiocarbanidin. When given orally to H37Rv-infected guinea pigs, thiocarbanidin was most effective in a dosage of 40 mg. per kilogram of body weight per day. When used in combination with streptomycin or isoniazid, it was superior to either streptomycin or isoniazid alone. Isoniazid alone was superior to the combination of thiocarbanidin and streptomycin, but not quite so effective as the combination of thiocarbanidin and isoniazid. Rabbits with miliary tuberculosis were benefited by thiocarbanidin, whereas aminosalicylic acid was ineffective. On a weight-for-weight basis, considerably less thiocarbanidin was necessary than aminosalicylic acid to produce an equivalent antituberculous effect in guinea pigs. Thiocarbanidin had little effect upon an infection produced by H37Rv thiocarbanidin-resistant tubercle bacilli. Thiocarbanidin showed no gross toxicity for rabbits or guinea pigs.

Meprobamate Addiction. R. C. Mohr and B. T. Mead. New England J. Med. 259:865-868 (Oct. 30) 1958 [Boston].

The authors report on a 36-year-old man addicted to meprobamate with obvious tolerance, dependence, and severe withdrawal symptoms. The patient was admitted to a Veterans Administration hospital in Salt Lake City with the chief complaint of confusion, marked tremor, and anxiety. He was an alcoholic, and in an attempt to stop drinking he began taking barbiturates, to which he became addicted. On 2 occasions, when he was unable to obtain barbiturates, he had grand mal seizures. For 2 years he was abstinent from alcohol and barbiturates and supported himself as an insurance executive. Owing to "nervousness from overwork" and on the prescription of a physician, he began taking meprobamate, 400 mg., 3 or 4 times a day. He responded to the medication, but to sustain the desired medicinal effects, an increasingly larger amount of the medicament was required. Tremors and anxiety resulted when voluntary withdrawal from the drug was attempted. It became necessary for the patient to take several tablets during the night to ensure adequate sleep. He began to loose weight and became increasingly irritable and ineffectual in his work. When admitted to the hospital he was consuming regularly 50 400-mg. tablets of meprobamate every 24 hours. During the period of heaviest medication he had been either extremely anxious or semistuporous. In a last attempt to "get off the drug" he became extremely tremulous, and about 20 hours after he stopped taking the drug he had a grand mal seizure. On hospitalization his gait was found to be shuffling and ataxic. Three hours after a mental, physical, and neurological examination a typical and severe grand mal seizure occurred, and the meprobamate medication was reinstituted, with doses of 1,200 mg. every 6 to 8 hours. The tremors and hyperreflexia subsided, and gradual withdrawal of the drug was accomplished without further incident.

Meprobamate has been accepted as a medicament for many conditions marked by tension and anxiety. It is relatively nontoxic, but toxic reactions have occurred, and at least one death has been reported. Toxic reactions have included chiefly mild to severe skin reactions and mild to severe psychic reactions. Addiction to meprobamate, though infrequently reported, is a very real possibility and deserves increased concern. Meprobamate should be prescribed with extra caution to any patient with a history of alcoholism or other addiction. When addiction to meprobamate is suspected, gradual and controlled withdrawal from the medication is probably the treatment of choice.

Topical Administration of Prednisolone in Treatment of Pleural Effusion Attributed to Pulmonary and Pleuropulmonary Tumors. F. Claudio and E. Percesepe. Riforma med. 72:1095-1103 (Sept. 27) 1958 (In Italian) [Naples].

Twenty patients of both sexes, aged between 34 and 72 years, with considerable pleural effusion attributed to pulmonary and pleuropulmonary primary or secondary neoplastic lesions were placed on prednisolone therapy, the drug being administered in doses of from 50 to 75 mg. for a maximum period of 30 days. Thoracentesis supplemented this therapy in some instances. Prednisolone therapy brought about a more frequent disappearance of the effusion, which also became clearer in color and consistency. Subjective and objective improvements of the symptoms, supported by roentgenologic findings, were observed in 14 patients (70%). The patients obtained relief from cough, pain, dyspnea, insomnia, and tachycardia. Cyanosis and swelling of the veins of the neck disappeared when they were present. Roentgenray pictures showed reexpansion of the pulmonary parenchyma in those instances in which the lungs were collapsed. Complete or considerable subsidence of effusion was obtained in patients who benefited from prednisolone therapy. Improvement or cure of effusion was confirmed during the follow-up examination. Disappearance of the effusion permitted a more effective application of roentgenotherapy, which was the only feasible therapeutic procedure for treatment of advanced malignant tumors in this series of patients. No undesirable side-effects to prednisolone were noted.

Clinical Evaluation of Chlorisondamine (Ecolid) in the Treatment of Hypertension. M. J. Kert, R. A. Nordyke, M. D. Shickman and others. Angiology 9:303-305 (Oct.) 1958 [Baltimore].

The authors report on 36 patients of advanced age with sustained elevations of blood pressure who were treated with chlorisondamine (Ecolid) chloride. The average blood pressure of these patients before the institution of treatment was 212/130 mm. Hg. The initial dose of the drug administered was 25 mg. every 12 hours, to be increased in increments of 25 mg. each dose until an effect was observed on the blood pressure or undesirable side-effects prevented further increase. Later in the study the starting dose was decreased to 12.5 mg., and at this dose no side-effects were observed. Eight patients received the drug for less than one month and were therefore excluded from the analysis of effects of the drug on the blood pressure. The remaining 28 patients received the drug for periods ranging from 1 to 13 months. Eleven (40%) of the 28 patients had a drop in diastolic blood pressure of from 10 to 30 mm. Hg or more. Excellent blood pressure responses were obtained in 6 of the 11 patients. A 12-hour dose schedule of chlorisondamine proved satisfactory. Undesirable side-effects, such as constipation, blurred vision, dizziness, weakness, syncope, and nausea, occurred in 20 of the 28 patients but were mild in most of them. For this reason, chlorisondamine would appear to be indicated chiefly in patients with severe hypertension. Orthostatic hypotension with syncope, the most serious side-effect, can be prevented by careful titration of the dose and administration of the drug after the morning and evening meals. In this respect, a small starting dose of 10 or 12.5 mg. is desirable. Careful supervision and instruction of the patient are essential for successful therapy of hypertension with chlorisondamine.

Disseminated Coccidioidomycosis Treated with Amphotericin B. R. C. Hunter Jr. and E. S. Mongan. U. S. Armed Forces M. J. 9:1474-1486 (Oct.) 1958 [Washington, D. C.].

Amphotericin B is an antibiotic derived from a species of Streptomyces organisms found in a soil sample from the Orinoco River basin in Venezuela. In vitro, it has been shown to have antifungal properties for a wide variety of organisms, including Coccidioides immitis. In vivo, it has had an ameliorating effect on mice experimentally infected with C. immitis. Since Amphotericin B became available to the authors more than a year ago, they observed 9 patients with disseminated coccidioidomycosis. Five were excluded from this study for various reasons, but the other 4 were treated with Amphotericin B. To 1 of these 4 patients with disseminated coccidiodomycosis Amphotericin B was given by mouth for 38 days. Although the patient recovered, the authors were unable to draw any conclusions on this mode of administration. To the other 3 patients Amphotericin B was given by intravenous injection. These 3 patients were treated for periods of 3 to 12 months. All improved, but the drug regularly caused chills, fever, anorexia, and nausea during and shortly after each infusion. Salicylates and antihistamines did not alter these reactions. Azotemia occurred one or more times in each patient on intravenous therapy but subsided upon interruption of treatment for 1 or 2 weeks. The unfavorable reactions were minimized by limiting the dose to 50 mg., given every other day immediately after supper. The water-soluble salt was dissolved in 5% dextrose solution to a concentration of 1 mg. per 10 ml. and was infused slowly. Six hours or more were taken for each infusion.

Seven coccidioidal abscesses in 2 of the patients were injected directly with 20 to 25 mg. of Amphotericin B dissolved in 2.5 ml. of solution. Two were injected once, 4 twice, and one 3 times, the injections being about one week apart. The abscesses had been present for several months and were either stationary or increasing in size when injected. The response was uniformly favorable, and fluctuation disappeared in 3 to 6 weeks. Amphotericin B appeared to be an effective agent for the treatment of disseminated coccidioidomycosis. Its toxicity limited the dosage, which, in turn, may have limited its effectiveness.

PATHOLOGY

Anastomosis in the Coronary Circulation. W. Laurie and J. D. Woods. Lancet 2:812-816 (Oct. 18) 1958 [London].

In a study of coronary heart disease among the Bantu of Natal, Union of South Africa, the authors investigated the presence of capillary and precapillary anastomoses between branches of the same coronary artery as well as between branches of both coronary arteries, with the aid of Schlesinger's perfusion technique. Eighty-seven normal hearts and 63 diseased hearts, obtained at routine consecutive autopsies of male and female patients, ranging from newborn premature infants to 85-year-old adults, were studied. In both normal and diseased hearts it was necessary to give a rough quantitative estimate of the degree of anastomosis present. Consequently the degrees of anastomosis were graded as "nil," "a quarter," "half," "three-quarters," and "complete." This grading was done by comparison of the anastomosis under review with a picture of a well-filled coronary tree of the same side, i. e., a coronary tree perfused from its own ostium. Eighty-two of the 150 hearts were perfused from the right side and 68 from the left side of the heart; no difference was found in the results. Functionally significant anastomoses (i. e., grade half or more) were found in 75% of the normal hearts from persons over 4 years of age, but in only 23% of the hearts from patients with chronic ischemic heart disease. Functionally significant anastomoses were found even in the hearts of some infants without cardiac disorder, the youngest of whom was 9 months old. There was no anastomosis in the heart of a patient with gross chronic myocardial ischemia. The likeliest explanation for these findings is that most of the healthy persons have a functionally important inherited coronary anastomotic blood supply; this inherited anastomosis probably protects some against ischemic heart disease and may modify ischemic heart disease in others. According to an addendum, this investigation still continues; among a total number of 350 hearts which have been perfused to date, complete anastomosis has been found in hearts from 3 newborn infants less than 21 days of age. These later findings support the explanation given for the earlier ones.

Cancer, Coronary Artery Disease and Smoking: A Preliminary Report on Differences in Incidence Between Seventh-day Adventists and Others. E. L. Wynder and F. R. Lemon. California Med. 89:267-272 (Oct.) 1958 [San Francisco].

Smoking is suspected of playing an important etiological role in the development of cancer and coronary artery disease. This prompted the authors to study the incidence of these diseases among Seventh-day Adventists, a religious group refraining from smoking and drinking. The records of 8 Seventh-day Adventist hospitals, whose patients include 8,128 who were non-Seventh-day Adventists and 564 who were members of the Seventh-day Adventist Church, were analyzed. The total number of cases reviewed (both male and female patients) was 3,679 for cancer, 3,082 for coronary artery disease, and 1,931 for myocardial infarction. Fifty-two per cent were patients from hospitals in the Los Angeles area. Seventh-day Adventist men and women from these hospitals were interrogated to obtain information about their background and environmental habits. Very few of the women smoked. Of the men, 72% over the age of 40 had never smoked, and 23% had smoked for less than 20 years; thus, only 6% of the Seventh-day Adventist men had a smoking history of more than 20 years, which compares with 85.4% in a sample of the general population. Therefore, so far as long-term smoking habits are concerned, the Seventh-day Adventist men can be compared with the women in the general population. Seventy-seven per cent of the men never drank alcohol, and only 0.5% admitted occasional drinking. The dietary intake of the Seventh-day Adventists differed from that of the general population only in a lower intake of meat, coffee, and tea and a higher intake of milk.

Assuming that the Seventh-day Adventists have the same chance of epidermoid and nonepidermoid cancer appearing at a given site as the non-Seventh-day Adventists and that the Seventh-day Adventists are 8.8% of the non-Seventh-day Adventist hospital population, the reported data revealed that in this nonsmoking population lung cancer among men occurs at least 90% less often than in the associated general population, even though a majority of the nonsmoking population lives in smog-polluted areas of southern California. Thus, smog does not seem to play a significant role in the development of lung cancer. It has also been shown that in such a population lung cancer occurs equally in men and women. Dietary factors have not previously been shown to play a role in the development of lung cancer, and it cannot be assumed that they accounted for the difference observed here. The incidence of cancer of the mouth, larynx, and esophagus in the study group is reduced from the expected rates by at least 90%, and the incidence in the 2 sexes is equal.

It could be expected that conditions which relate to both smoking and drinking would be especially low in a population group which does neither. Dietary differences are not thought to account for the scarcity of upper respiratory and esophageal cancers in this group. Of particular interest was the lower incidence of coronary artery disease and myocardial infarction in the study group and the fact that this low rate is prominent in the younger men, whereas the incidence in the women was as expected. It seems reasonable to account for this lower incidence among men by their similarity to women in low-tobacco consumption. The present data are thus consistent with the findings presented by other investigators, showing smoking to be a factor in the development of myocardial infarction. This association is considered to be a precipitating factor rather than a causative one, as in the instance of cancer of the lung. Regardless of whether it is referred to as a precipitating or a causative factor, if tobacco increases the incidence of so important a disease as myocardial infarction, it is a matter of just concern.

Pathologic Anatomy of Experimental Leukemia Produced by Injection of Benzol Extracts from Organs of Leukemic Patients. M. P. Khokhlova. Blood 13:917-925 (Oct.) 1958 [New York].

This study from the Lenin Institute of Blood Transfusion and Hematology in Moscow deals with leukemia experimentally induced in animals by the injection of organ extracts from patients who had died of leukemia. By injecting mice with benzene extracts from organs of deceased leukemic patients, the author was able to produce both intramedullary and extramedullary myeloid hyperplasia, characteristic of leukemia. In most instances a leukemic blood picture accompanied these changes. Subsequent transfers both of tumor and visceral emulsions and blood from leukemic animals produced myelogenous leukemia in a number of instances. The positive transfer results seemed to confirm the presence of true leukemia. Only myeloid leukemia was evoked both in the original mice and the transfers, hemocytoblastic, myeloblastic, and myelocytic types being observed. The last-named type occurred most frequently.

When donor organs from patients with chronic leukemia were used, a myelocytic type of leukemia usually developed in the mice; with acute leukemia extracts, hemocytoblasts were always found. The development of experimental leukemia from donors with both chronic and acute leukemia indicates the identical nature of these processes. In some mice the author observed the development of a malignant tumor, usually at the injection site, and sometimes at a distance from it. Results showed that the injection of one and the same benzene extract can bring about leukemia alone, leukemia plus tumor, or tumor alone. Leukemias produced by the benzeneextract method and by use of chemically pure carcinogens were morphologically identical. Since both methods can induce malignant tumor formation together with the leukemia, this points to a close pathogenetic relationship of these diseases.

Keratoacanthoma: A Benign Cutaneous Tumor Arising in a Skin Graft Donor Site. J. H. Wulsin. Am. Surgeon 24:689-692 (Oct.) 1958 [Baltimore].

Wulsin reports on an 82-year-old man who had a fixed, firm mass overlying the left sternocleidomastoid muscle and apparently arising primarily in the skin. The lesion was superficially ulcerated and adherent to the underlying muscle. It had been slowly growing over a period of several years despite intermittent x-ray therapy. The diagnosis was basal-cell carcinoma. On Oct. 17, 1957, this tumor was excised with a margin of normal tissue. The pathological diagnosis of the resected tumor was basal-cell tumor with some squamous-cell elements. The defect created by the excision was covered with a thin, split-thickness skin graft taken from the anterior surface of the left thigh with a dermatome. The donor site was prepared by shaving and applying liquid petrolatum.

A small, firm, slightly tender, 1-mm. papule was first noted in the center of the healed donor site 22 days after the operation, and within one week it grew to 4 mm. The papule was incised in the belief that it represented a crusted pustule, but it proved to be solid. Over the next 4 weeks it grew rapidly and steadily into a single, firm, nonulcerated, slightly umbilicated nodule, about 15 mm. in diameter, and raised prominently above the skin. The patient complained about its being tender and sensitive to the friction of his trousers. Its rapid growth and clinical features suggested a malignant neoplasm of the skin arising in a donor site. On Dec. 4, 1957, the nodule in the donor site was excised. There was prompt healing without further tumor formation. The initial pathological diagnosis was squamous-cell carcinoma, but upon review of the histological sections the diagnosis of keratoacanthoma was established.

Keratoacanthoma (molluscum sebaceum) is a benign tumor of the skin. It resembles squamous-cell carcinoma of the skin both grossly and microscopically. The differentiation rests on the clinical rather than on the miscroscopic features. Rapid growth and spontaneous involution characterize the lesion. Usually single but occasionally multiple, it appears chiefly on exposed areas and has been noted particularly on patients working with petroleum products. To the author's knowledge, the case here reported is the first instance of such a tumor arising in a skin graft donor site. It is interesting to speculate whether the petroleum product, liquid petrolatum, or the trauma of removing the graft initiated its rapid growth. An accurate diagnosis of this tumor is important for prognostic as well as therapeutic reasons. Undoubtedly in the past many instances have been mistakenly labeled as squamous-cell carcinoma.

Thyroid Neoplasms Following Irradiation. G. M. Wilson, R. Kilpatrick, H. Eckert and others. Brit. M. J. 2:929-934 (Oct. 18) 1958 [London].

The authors report on 8 girls and women, between the ages of 10 and 63 years, and 1 25-year-old man with thyroid neoplasms, all of whom had been exposed several years previously to ionizing irradiation by radium or roentgen rays. A definite carcinoma of the thyroid was observed in 7 of the 9 patients, and an adenomatous enlargement of the thyroid in the remaining 2. In 6 of the 7 patients the irradiation was given in infancy or childhood for the treatment of cutaneous lesions in the neck, such as nevus, keloid, and eczema. In these 6 patients the carcinoma was predominantly papillary in type. The dose to the thyroid varied from 130 to 2,700 r, and the latent period varied from 5 to 18 years. The carcinoma developed in the part of the thyroid exposed to the greatest irradiation. The 7th patient had been irradiated in adult life for thyrotoxicosis, and an anaplastic carcinoma developed 37 years later. Of the 2 patients with adenomatous enlargement of the thyroid, one had had irradiation carried out in early infancy for a nevus overlying the left sternomastoid tendon, and the other was treated by roentgen-ray irradiation in early adult life for thyrotoxicosis. Histologically, hyperplastic adenomatous areas and mitotic figures were seen, but in the absence of local invasion and metastases the histological features alone did not justify a diagnosis of carcinoma. The lesions were regarded as premalignant conditions. Exposure in childhood to ionizing irradiation predisposes to the appearance of thyroid neoplasms. The association after irradiation in adult life is less certain.

Primary Lung Cancer and Pulmonary Tuberculosis: A Study Based on 570 Postmortem Examinations. K. Murasawa and V. Altmann. Sea View Hosp. Bull. 17:37-52 (July) 1958 [New York].

The interest of these authors in pulmonary tuberculosis and primary lung cancer was awakened by the observation that a number of cases diagnosed clinically as tuberculosis proved at autopsy to be primarily lung carcinomas. Some of these patients showed either mild active or more extensive progressive tuberculosis, but others had no active tuberculosis in the lungs. It seemed probable that there must have been some degree of tuberculosis in the lungs of all these patients, at least at the time of their admission to Sea View Hospital, Staten Island, N. Y., since the basis for entering the hospital was a sputum positive for acid-fast bacilli. In 570 consecutive autopsies performed during a 10-year period at this hospital, 39 cases of primary lung carcinoma were found. There was close anatomic association between active pulmonary tuberculosis and primary lung carcinoma in 14 instances, corresponding to about 2.4% of all cases. This figure corresponds to the one expressing the probability of developing cancer of the lung among a comparable average population. No etiological relationship was detected between lung tuberculosis and carcinoma. The authors believe that, if there is any increase in the frequency of lung cancer in tuberculosis hospitals, the reasons are other than a direct causal relationship between the two conditions.

RADIOLOGY

Clinical Picture and X-Ray Therapy of Acromegaly. E. N. Mozharova. Probl. endokrinol. i gormonoterap. 4:98-103 (No. 4) 1958 (In Russian) [Moscow].

The author presents the results of x-ray therapy of 110 patients with acromegaly who were examined clinically and then followed up for a prolonged period (up to 20 years) after the treatment. Deep x-ray therapy was employed. Various methods were developed and applied: irradiation of the hypophysial-hypothalamic area, of the superior cervical sympathetic ganglions, and of the thyroid gland, as well as treatment with radium by introducing it through the nasopharynx under the basilar portion of the sella turcica. These methods were used in various combinations. Different single and total doses were employed according to the indications. The clinical symptoms and the variations of the course of this disease (complications by thyrotoxicosis, diabetes mellitus, etc.) were taken into consideration. Radiation treatment of acromegaly gave successful results. A number of grave symptoms were relieved or completely disappeared even in complicated cases of acromegaly (for example, menstrual periods were reestablished, vision was recovered, and symptoms of diabetes and thyrotoxicosis disappeared). The patients were able to return to active life for many years. In individual approach, with the careful choice of the methods and doses, radiation treatment gives no complications and should be employed before surgery. The latter should be resorted to only in radioresistant cases of this disease.

Roentgen Examination of the Gastrointestinal Tract as an Aid in the Diagnosis of Acute and Subacute Reticuloendotheliosis. S. B. Feinberg and R. G. Lester. Radiology 71:525-533 (Oct.) 1958 [Syracuse, N. Y.].

According to the authors there have been many papers correlating Letterer-Siwe disease and Hand-Schüller-Christian disease and eosinophilic granuloma under the general designation of nonlipid histiocytosis, histiocytosis-X, or reticuloendotheliosis. Among the diagnostic criteria originally listed by Siwe, the gastrointestinal tract was not mentioned. This paper is particularly concerned with roentgenologic findings in the gastrointestinal tract. Two cases of reticuloendotheliosis recently observed at the University of Minnesota Hospitals in Minneapolis led to these studies. In the first patient, a 9-month-old infant, vomiting and abdominal distention developed at 2 months of age. At 3 months the classical papular eruptions appeared over the trunk and scalp. Abdominal ascites and dependent edema also developed. Adenopathy was an insignificant finding. On examination of the gastrointestinal tract, the small and the large intestine appeared moderately distended, suggesting adynamic ileus. Marked abnormality of the mucosa of the duodenal loop and proximal jejunum was obvious. The mucosal pattern was effaced in some zones and finely granular in others, suggesting hypertrophy and/or edema of the intestinal walls. Skin biopsy showed changes diagnostic of acute reticuloendotheliosis, e. g., heavy mononuclear-cell involvement. The bone marrow revealed large mononuclear reticulum cells and an increase in megakaryocytes. Lymph-node biopsies were negative. Laboratory studies showed hypoalbuminemia associated with protein loss and disturbed intestinal absorption. Postmortem findings included diffuse replacement of liver substance and thickening of the small intestinal wall by reticuloendothelial mononuclear-cell invasion.

These observations induced the authors to recall a child with subacute reticuloendotheliosis for examination of the gastrointestinal tract. She had survived 28 months with middle-ear involvement, recurrent lymphadenopathy, and massive bone invasion but without gastrointestinal symptoms. Nevertheless, a survey of the small intestine showed absence of normal mucosal pattern, segmentation of intestinal loops, and barium flocculation interpreted as representing mesenteric node involvement. In view of the findings in these 2 cases, the records of the University of Minnesota Hospitals were reviewed. Twenty-two cases of reticuloendotheliosis were found in the files. In 11 of these patients the condition was acute, and 7 of them had intestinal and/or mesenteric node invasion. Six of the 7 patients had had clinical symptoms of the gastrointestinal tract. More than 20% of the verified cases in a survey of the literature had autopsy evidence of intestinal and/or mesenteric node involvement. The authors advocate routine upper gastrointestinal tract examination as an aid in the diagnosis of atypical reticuloendotheliosis in which vomiting and diarrhea may be the only clinical symptoms.

Pericardial Celomic Cyst: A Re-Evaluation. G. F. Lull Jr. Radiology 71:534-541 (Oct.) 1958 [Syracuse, N. Y.].

The entity of pericardial celomic cyst was established by Lambert in 1940; this investigator also suggested a theory of its origin, postulating the persistence, as a separate cavity, of one of the mesenchymal lacunae which in the developing embryo fuse to form the pericardial celom. He indicated that the distinction between pericardial celomic and lymphangiomatous cysts could not be made on a histological basis, since it is impossible to distinguish between mesothelium and endothelium. His premise that multilocularity in thin-walled cysts excludes pericardial celomic cysts and indicates lymphangiomatous cysts is rejected by the present author, who reviews observations on 15 patients in whom pericardial celomic cysts were pathologically proved. These patients were seen on the radiology service of the Fitzsimons Army Hospital in Denver. The roentgenologic diagnosis of pericardial celomic cyst is difficult in view of the various types of congenital cysts which may be present in the same area, namely, epidermoid, dermoid, teratoid, bronchial, esophageal, gastroenteric, pericardial celomic, and lymphangiomatous cysts. Some of the data on the 15 patients with pathologically proved pericardial celomic cysts are tabulated, but detailed reports are not given, because 12 of the 15 cases had been reported before.

In addition to the 15 patients with pericardial celomic cysts, 7 with anterior mediastinal lesions were reviewed in an attempt to find roentgenographic similarities or differences. Two of these 7 patients had lymphangiomatous cysts which proved to be unilocular rather than multilocular, whereas 2 of the 15 pericardial celomic cysts were multilocular. The criteria for the diagnosis of pericardial celomic cyst include a thin cyst wall, clear fluid contents, a lining of flattened cells that have the appearance of endothelium or mesothelium, and absence in the wall of any elements indicating lymphangiomatous or other etiology. An awareness that the cyst wall and its contents may be altered by inflammatory reaction in the adjacent tissues will be helpful. Attention should be paid to the margins of the lesion. If there is a fairly sharp angle at the border of the area of density where it merges with the heart, then the mass probably is separate from the heart. If an acute angle does not exist, then the lesion is probably intimately incorporated with or lies within the pericardium, and the diagnosis of pericardial celomic cyst should be viewed with suspicion. The demarcation sign proved of value in the differential diagnosis of localized pericarditis and pericardial fat pad.

While Lambert's theory of the etiology of these cystic lesions explains why they can be present, it does not account for the time of their appearance or the mechanism by which they are produced. Since 3 patients had a history compatible with respiratory tract infection and 1 had a history of injury while boxing, it is postulated that the trigger mechanism must be some form of injury, either in the form of inflammatory disease or trauma. In those patients who were asymptomatic, the injury was probably not of a sufficient degree to have been incapacitating or to have been remembered. This does not preclude the fact that the cysts themselves may be responsible for some of the symptoms.

PUBLIC HEALTH

Evaluation of the Effectiveness of Anti-Influenza Vaccination. V. Pavilanis, A. Frappier, F. Somlo and others. Canad. M. A. J. 79:527-532 (Oct. 1) 1958 [Toronto].

The authors attempted during the winter of 1954-1955 to assess the degree of protection conferred by a polyvalent anti-influenza vaccine. Describing the preparation of the vaccine, they say that after the period of incubation the allantoic fluid was collected aseptically, and the virus which had multiplied within it was purified and concentrated by centrifugation. After treatment with formol 1 in 4,000, the agglutinating power of each monovalent vaccine was adjusted by dilution to 500 units per cubic centimeter. The 4 monovalent vaccines were mixed in the following proportions: PR 8, 22.2%; FMI, 22.2%; Cuppett, 22.2%; and Lee, 33.3%. The protection conferred by this vaccine was studied in the following 4 groups: 1. At a psychiatric hospital 2,862 patients were given the vaccine and 748 a nonvirulent liquid (placebo); 1,077 patients served as nonvaccinated controls. 2. Among civil service employees of the city of Montreal, 558 were given the vaccine and 476 the placebo fluid; 2,466 individuals were used as nonvaccinated controls. 3. In a Montreal factory the vaccine was given to 313 workmen and the placebo solution to 277 others. 4. At Montmagny, a semirural area situated 40 miles down the St. Lawrence from Quebec, the vaccine was administered to 1,525 children and 236 adults; 558 children and 195 adults were given injections of placebo.

An epidemic of mild influenza affected Montreal in March, 1955, and its origin was traced to a virus of antigenic structure identical with that of influenza virus, type A, strain Cuppett/50. The quadrivalent vaccine given in this study led to an appreciable production of antibodies; their titer was quadrupled for strains PR 8 and Lee, the response being much weaker with strains FMI and Cuppett. This quadrivalent vaccine conferred a protection against clinical influenza varying between 40 and 80% according to the group.

Copper Poisoning from Vending Machines. S. H. Hopper and H. S. Adams. Pub. Health Rep. 73: 910-914 (Oct.) 1958 [Washington, D. C.].

Several health departments have reported cases of illness that appear to be copper poisoning associated with carbonated drinks obtained from vending machines. These machines, the post-mix type, release 1 oz. of a flavored sirup into a cup and then add 5 oz. or more of carbonated water. After presenting cases of copper poisoning, the authors discuss previous reports on the toxicity of copper. There seems to be no unanimity of opinion regarding the toxicity of this metal. It has been said that the danger from copper water-supply lines is slight. Copper is readily attacked by the various acids present in foods, such as acetic, citric, malic, tartaric, and oleic acids. Consequently, any food or drink containing acid will dissolve a certain amount of copper if it comes in contact with that metal. There is no doubt that the human organism can take care of minute amounts of copper, but where the dividing line is between harmless and harmful amount cannot yet be said. Individual susceptibility probably enters to complicate the problem.

Studies were carried out with a post-mix type of vending machine. If the check valves in such a machine do not function correctly, carbon dioxide may enter the water-supply line. In the event that this line is made of copper, then (*a*) the carbon dioxide or carbonated water will react with the copper; (*b*) under certain conditions the quantities of copper going into solution could be quite large; and (*c*) copper poisoning could occur from a beverage dispensed from a post-mix type of carbonated beverage machine. The authors feel that copper poisoning does not represent a public health problem of any great magnitude, since the relatively few cases on record, compared with the millions of soft drinks consumed, would give an infinitesimally small case rate. To minimize copper poisoning, however, they make the following suggestions: 1. Vending machines should adhere to the sanitation code concerning the use of 2 check valves or a double check valve, an air gap, a device to vent the carbon dioxide to the atmosphere, or a device approved by the health authority. 2. A carbonator should not be made of copper; it should be made of an acid-resistant nontoxic metal. 3. Water filters and water-conditioning devices should not use a copper container.

BOOK REVIEWS

Heart Disease and Pregnancy: Physiology and Management. By C. Sidney Burwell, M.D., Samuel A. Levine Professor of Medicine, Harvard University, Boston, and James Metcalfe, M.D., Associate in Medicine, Harvard University. Cloth. $10. Pp. 338, with 45 illustrations. Little, Brown & Company, 34 Beacon St., Boston 6; J. & A. Churchill, Ltd., 104 Gloucester Place, Portman Sq., London W. 1, England, 1958.

The authors of this admirable book dedicated themselves to the premise "that an understanding of normal physiology enables management of disease during pregnancy to be rational rather than empirical." This premise is ably and clearly developed. This book should be required reading for all senior medical students and should be equally valuable to every physician responsible for the care of pregnant women, whether he is an obstetrician, general practitioner, internist, or cardiologist. The authors not only develop a sound basis for understanding the impact of pregnancy on the circulatory system but also cover in detail the successful management of all forms of acquired and congenital heart disease during pregnancy. The indications for interruption or prohibition of pregnancy are clearly set forth.

Progress in Radiation Therapy. Edited by Franz Buschke, M.D., Professor of Radiology, University of California School of Medicine, San Francisco. With 13 contributors. Cloth. $9.75. Pp. 284, with illustrations. Grune & Stratton, Inc., 381 Fourth Ave., New York 16; 99 Great Russell St., London, W. C. 1, England, 1958.

This initial volume in a projected series contains reviews on a variety of subjects designed to establish a foundation for future reports. Subjects are presented in the biological, physical, clinical, and educational fields that have direct application to clinical radiation therapy. At the beginning of this volume are two excellent chapters on the history of radiation therapy and of radiation sources for cancer therapy. The basic biological problems that are critically surveyed include the radiobiological effectiveness of radiation from different external sources, the relationship of the radiation dosage to time, and the modification of radiation effects by chemical means. The last half of the book is largely concerned with clinical problems; it covers ultrafractionation, radioresistant versus radiosensitive carcinomas of the cervix and their recognition by cytological means, renal embryoma, malignant intracranial neoplasms, central nervous system tolerance to radiation, carcinoma of the thyroid, and nonmalignant diseases of the eye. The last chapter deals with radiation therapy as a medical specialty, and a plea is made for the separation of radiation therapy from the field of general radiology. All subjects have been critically and thoroughly reviewed. Each chapter is accompanied by an excellent bibliography. This book should be of interest to radiation therapists as well as general radiologists. It fills a distinct and long-felt need.

Emergency Treatment and Management. By Thos. Flint Jr., M.D., Director, Division of Industrial Relations, Permanent Medical Group, Oakland and Richmond, California. Second edition. Cloth. $8. Pp. 539. W. B. Saunders Company, 218 W. Washington Sq., Philadelphia 5; 7 Grape St., Shaftesbury Ave., London, W. C. 2, England, 1958.

This book consists of three general divisions: general medical principles and procedures; emergency treatment of specific conditions; and administrative, clerical, and medicolegal principles and procedures. It is compact and easily transportable. The specific topics are numbered and the sections on diagnosis and emergency treatment are readable and in outline form. The book covers most common emergencies in internal medicine, general and traumatic surgery, pediatrics, and obstetrics that would be met in the office, hospital emergency room, or the home. The specific emergencies are covered in a concise manner devoid of controversial points for the sake of brevity. In some instances only one treatment is suggested, thus unintentionally implying that no other methods are acceptable. The section on acute poisoning is excellent. It provides an extensive list of common poisons with their characteristics, symptoms, and treatment. A list of the toxic ingredients in a wide variety of commercial preparations is also included. This volume should prove particularly useful to interns, residents, and physicians treating emergencies.

Essentials of Gynecology. By E. Stewart Taylor, M.D., Professor and Head of Department of Obstetrics and Gynecology, University of Colorado School of Medicine, Denver. Cloth. $12. Pp. 502, with 347 illustrations. Lea & Febiger, 600 S. Washington Sq.,Philadelphia 6, 1958.

This new textbook is unusually well presented from the standpoint of subject matter, illustrations, and writing. The arrangement of topics follows the generally accepted teaching schedule, and the book should find a useful place in medical schools. Gynecology is here presented in a broad manner. Use of this book should be supplemented with an intensive course in regional pathology.

These book reviews have been prepared by competent authorities but do not represent the opinions of any medical or other organization unless specifically so stated.

QUESTIONS AND ANSWERS

EXCESSIVE GROWTH IN TWELVE-YEAR-OLD GIRLS

To the Editor:—*A patient is concerned about the excessive growth of her daughter, who, at the age of 12 years, is 5 ft. 7½ in. (171.4 cm.) tall and weighs 130 lb. (59 kg.). Out of the 180 children in her gymnasium class in junior high school, she is the tallest. The mother is concerned because the child appears to be developing a great deal of self-consciousness and shyness because of her tall stature. Is there any recognized safe therapy, including hormone therapy, which can be used to stop growth in such a child? It should be noted that the child is taller than either of her parents, any of her grandparents, and both of her older siblings. There is no evidence to date indicative of a pituitary adenoma.*

William H. Davis, M.D., Los Angeles.

To the Editor:—*Please give advice as to the best hormonal regimen to arrest or retard growth in a 12-year-old girl who already has attained a height of 5 ft. 5 in. (165.1 cm.). She has not started her menses. Findings on physical examination were within normal limits, except for the height. Her weight was 105 lb. (47.6 kg.). The bone age was found to be consistent with the chronological age. The girl's father and mother are 6 ft. 5 in. (195.6 cm.) and 5 ft. 10 in. (177.8 cm.) tall respectively; her 18-year-old brother is 6 ft. 4 in. (193 cm.) tall, and her sisters, 21 and 23 years of age, are 5 ft. 10 in. and 5 ft. 8 in. (172.7 cm.) tall respectively. Should estrogens be used alone or together with androgens, and what is the recommended dosage?*

Warner M. Soelling, M.D., Modesto, Calif.

Answer.—In reference to the girl in the first question, hormone therapy might be justified in an attempt to slow her linear growth. A further increase of at least 3 to 4 in. (7.6 to 10.1 cm.) can be expected in the next six years. This may add to the personality difficulties that have already developed. However, x-ray of the long bones for bone age is indicated for comparative purposes during and after treatment. Furthermore, no mention is made of the presence or absence of secondary sex characteristics. This is important because with minimal or no secondary sex characteristics a more prolonged growth period may be anticipated, whereas if she is going through puberty growth may cease spontaneously in a shorter period of time. Thus, if hormone therapy is used, the dosage and duration of therapy will relate to the degree of maturity present when the drug therapy is introduced. With respect to the girl in the second question, retarding of growth at this time should not be attempted unless there are definite indications. There is a definite family pattern of growth in this instance, and it is assumed that the child is fairly well adjusted, having tall parents and older sisters. It would be interesting to know the attitude of her mother and sisters with respect to their large size and whether they are well adjusted. If this child has personality difficulties, as in the case of the child in the first question, then hormone therapy may be justified. Although it is stated that findings on physical examination were within normal limits except for height, more information relative to secondary sex characteristics would be helpful.

Treatment of excessive growth in such cases is best accomplished with estrogens, either in the form of diethylstilbestrol, 1-2 mg. daily, or conjugated estrogens, 2.5-5 mg. or, if necessary, up to 10 mg. daily. The latter dose is seldom required unless uterine bleeding occurs during treatment. If, in spite of increasing doses of estrogens, bleeding continues, testosterone propionate, 25-50 mg. given intramuscularly, may be used, followed by a short course of therapy with methytestosterone, 10-30 mg. per day given orally. It may be necessary to continue estrogen therapy for one to three years or longer. There are no harmful effects of prolonged estrogen therapy in such patients. The rapid development of secondary sex characteristics and the probability of irregular uterine bleeding during treatment should be explained to both the parents and the child.

FORCE TO DISRUPT OSSICULAR CHAIN

To the Editor:—*Has any material been published regarding the amount of force necessary to disrupt the various joints and tendons of the middle ear? Construction of an instrument is being considered with use of the Schiøtz tonometer principle except with a pull instead of a push, which will enable a large series of studies to be done in fresh postmortem specimens and in operative cases.*

Glenn J. Greenwood, M.D., Los Angeles.

Answer.—The structure of the ossicles, and particularly of the stapes, is so variable, as has been shown by clinical observation and the anatomic

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The answers here published have been prepared by competent authorities. They do not, however, represent the opinions of any medical or other organization unless specifically so stated in the reply. Anonymous communications cannot be answered. Every letter must contain the writer's name and address, but these will be omitted on request.

studies by Professors Barry Anson and Theodore Bast of the Northwestern University and the University of Wisconsin, that it would be difficult to determine a particular force necessary to disrupt the ossicular chain. It could hardly be determined in the cadaver ear, and there have been no published reports of such studies on the living patient.

ATOPIC DERMATITIS AND CLIMATE

To the Editor:—*A 7-year-old boy has had atopic dermatitis since birth. In the past two years his condition has become severe, involving the upper and lower extremities, neck, groin, and other areas of his body. Pruritus is present day and night. Medicaments of all kinds, given orally and topically, have not given any relief. The child is a resident of the Northeast, and, during a trial visit to Denver, Colo., for two weeks, he showed remarkable improvement. Please give information with regard to relief obtained in dry climates. What particular areas would be recommended?*

M.D., Florida.

Answer.—Atopic dermatitis of the extent and severity described in this child is a particularly distressing and difficult medical problem, to patient and parents alike. In addition to the discomfort of incessant itching, and the cosmetic disfigurement produced by the dermatitis, such patients are prey to the development of other manifestations of atopy. Also, the bacterial flora of the skin is abnormal, and chronic staphylococcic infection seems to pose a problem of increasing significance in some such patients. There can be no question that climatological therapy is frequently helpful, sometimes to the point of disappearance of all signs and symptoms of atopic dermatitis. It is often entirely comparable to the effects of steroid therapy and, of course, far less dangerous. In general, patients with atopic dermatitis are better in a warm but not excessively hot environment, where periods of prolonged high humidity are not encountered. Such patients sometimes do well in southern Florida or California. Others seem to obtain more benefit from a drier warm climate, such as is found in some localities in the Southwest United States. As a rule, opportunity for plenty of exposure to natural sunlight is an advantage. The climate of Denver, Colo., during the warm months of the year is often beneficial, but recurrences might well be noted during the cold winter season, when exposure to natural sunlight is not possible and when woolen clothing must be worn. On the other hand, chronic severe atopic dermatitis is encountered in all localities in the United States with some frequency, and it is therefore clear that climatological therapy is not always successful. Though such treatment involves a financial burden and disarrangement of families, it is well worthwhile when successful in severe prolonged atopic dermatitis. Some such patients, if the skin remains clear for several months, may then tolerate their home environment without too much difficulty; in others this is not the case.

CAISSON DISEASE AND PITUITARY ADENOMA

To the Editor:—*A patient has adenoma of the pituitary gland, confirmed by x-ray findings and visual field report. He was a deep sea diver from 1941 to 1946. Is there any causal relationship between caisson disease with its subsequent possible complications and the present adenoma of the pituitary gland?*

Aaron M. Spirer, M.D., New York.

Answer.—There is no evidence that caisson disease with its subsequent possible complications is in any way related causally to adenoma of the pituitary gland.

BILIARY CIRRHOSIS AND COLITIS

To the Editor:—*In the Questions and Answers section of* The Journal, *Nov. 1, 1958, page 1297, an inquiry was made concerning the efficacy of steroid therapy in a patient with massive ascites, abnormal liver function, and ulcerative colitis. It should be pointed out that during the past several years a number of communications have been published on the subject of liver disease and ulcerative colitis. In a recent paper, Gray and colleagues* (Am. J. Digest. Dis. 3:481, 1958) *discuss this association and also indicate a possible relationship of these two disease processes to systemic lupus erythematosus. In the case under discussion, the ascites could be caused by cirrhosis of the liver with portal hypertension but it could also be a manifestation of the serous membrane involvement of systemic lupus erythematosus. The age and sex of the patient favor this concept. That steroid therapy may be of benefit in such cases is suggested by the results obtained by Gray and co-workers. They reported moderate to excellent responses to cortisone in five of eight patients with hepatitis, ulcerative colitis, and (in four of the eight) positive L. E. test results.*

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SIMPLE, RAPID DIAGNOSTIC TEST FOR RHEUMATOID ARTHRITIS—BENTONITE FLOCCULATION TEST

Kurt J. Bloch, M.D.
and
Joseph J. Bunim, M.D., Bethesda, Md.

THE presence of an unusual serum protein capable of reacting with gamma globulin is among the most constant laboratory findings in rheumatoid arthritis. The demonstration of this substance (often referred to as the "rheumatoid factor") by various serologic tests is included in the list of criteria required for the diagnosis of "definite" rheumatoid arthritis proposed by the American Rheumatism Association. It is known that the presence of the rheumatoid factor is closely associated with the finding of subcutaneous nodules, erosion of joint cartilage, and destruction of subchondral bone.[1] Duthie and co-workers[2] found that the presence of the rheumatoid factor seemed to be related to prognosis. In their patients who had positive findings, the disease followed a more severe course than in those with negative findings. In studies of the epidemiology of rheumatoid arthritis in various population groups, the serologic test has been found especially useful and dependable as a diagnostic aid.[3]

Several laboratory procedures are now available for the demonstration of the rheumatoid factor. Despite the importance of serologic testing in diagnosis, prognosis, and epidemiology of rheumatoid arthritis, there are relatively few laboratories in the United States in which these tests are performed.

The bentonite flocculation test (BFT) is a modification of a serologic test used to detect Trichinella antibodies. Ingredients for the test are readily available from commercial sources. Stock preparations are stable for months. Equipment necessary for this test is available in the average clinical laboratory. Minimal technical skill is required for performance of the test and reading of results. One hour or less is required from receipt of the serum to completion of the test. Of 114 patients with verified rheumatoid arthritis, the test finding was positive in 85%. Disseminated lupus erythematosus and scleroderma contributed the next highest percentage of positive tests, 55% and 50% respectively. In 58 patients with nonrheumatoid arthritis, the test finding was positive in 3 (5%). The BFT result is positive in about 10% of syphilitic as well as biological false-positive serums.

Among the major deterrents to wider application of these serologic tests have been (1) complex and unstable ingredients, such as sheep erythrocytes

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From the National Institute of Arthritis and Metabolic Diseases, National Institutes of Health.

and rabbit anti-sheep-erythrocyte serum; (2) complex procedures, such as absorption of heterophil agglutinins from human serum, fractionation of serum, and tanning of sheep erythrocytes; (3) time consumption (performance of 20 tests may fully occupy a skilled technician for several days); and (4) difficulties in reading end points of agglutination (this requires considerable experience).

Bentonite Flocculation Test

The bentonite flocculation test (BFT) is a simple, rapid, sensitive procedure for the detection of the rheumatoid factor.[4] Bozicevich and associates,[5] in 1951, described a serologic test with bentonite particles coated with antigenic material from Trichinella used to detect antibodies in the serum of patients infected with Trichinella. The BFT is a modification of this technique, with human gamma globulin used as the coating agent. Ingredients for the test are readily available from commercial sources. Stock preparations are stable for months. Equipment necessary for this test is available in the average clinical laboratory. Minimal technical skill is required for performance of the test and reading of results. One hour or less is required from receipt of the serum to completion of the test.

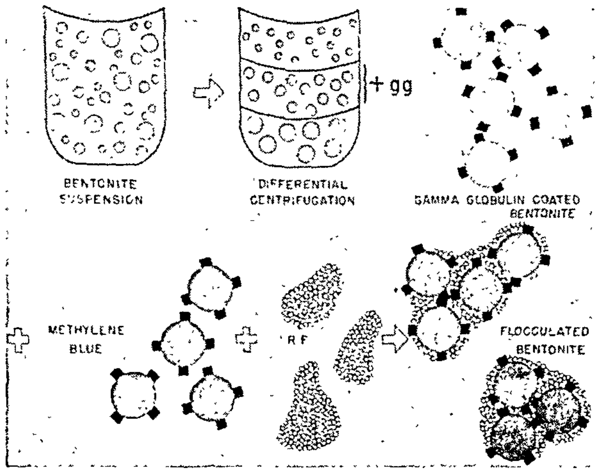

Fig. 1.—Schematic outline of bentonite flocculation test. Bentonite particles are suspended in water and optimum particle size obtained by differential centrifugation. Particles are coated with gamma globulin and dyed with methylene blue. Rheumatoid factor, present in patient's serum, flocculates coated particles.

A schematic outline of the BFT is presented in figure 1. Wyoming bentonite, a naturally occurring clay in powder form, is suspended in distilled water. Particles of optimum size for the test are obtained by differential centrifugation. These are coated with pooled normal human gamma globulin. Methylene blue is added to stain the particles and make them readily visible. The coated ("sensitized") bentonite particles are then added to serial, twofold, saline dilutions of inactivated serum on routine serology slides. These slides then are placed on a Boerner type of rotating machine for 20 minutes, and results are observed under a microscope at low-power magnification. Findings on the flocculation test are considered positive when at least 50% of the bentonite particles are clumped into compact masses by a serum diluted 32 times (1:32) or more. In negative results the particles remain freely suspended.

Several thousand tests have been performed in our laboratory. The stock bentonite suspension is stable for six months and the gamma globulin solution for two to three months. Although we prepare freshly coated bentonite particles every week, it has been found that coated particles may be used satisfactorily after three weeks' storage in the refrigerator. Sufficient stock bentonite solution can be prepared at one time to permit the performance of 500 screening tests.

How to Perform the Test

Preparation of Stock Bentonite Suspension.—Detergents (often used in cleaning glassware) adherent to the surface of glassware will interfere with this test. It is important, therefore, to cleanse all glassware of this material by washing with distilled water before using.

Suspend 0.5 Gm. of Wyoming bentonite (BC micron or no. 200 standard Volclay) in 100 ml. of distilled water. Homogenize in Waring blendor for one minute; repeat after five minutes for one minute.

Transfer bentonite suspension to 500 ml. glass-stoppered graduate, and add distilled water to make 500 ml. Shake thoroughly, and allow to settle for one hour. Pour off supernatant into six 100-ml. centrifuge tubes (heavy duty, Pyrex), and centrifuge, by tachometer, at 1,300 rpm for 15 minutes. Use International centrifuge, size 2, with no. 240 head. Pour off and save supernatant; discard sediment.

Centrifuge supernatant in 100-ml. tubes at 1,600 rpm for 15 minutes. Pour off supernatant, and discard it.

Resuspend accumulated sediment from the six tubes in 100-ml. of distilled water, and homogenize in Waring blendor for one minute. This is the stock bentonite suspension, which, in our experience, has remained stable for as long as six months without losing its adsorptive properties.

Preparation of F-2 Solution.—Lyophilized fraction 2 (gamma globulin), 0.5 Gm., derived from pooled normal human serum, is suspended in installments while stirring in 50 ml. of 0.06 M barbital (Veronal) buffer, pH 8.6 (made by dissolving 0.184 Gm. of barbituric acid and 1.03 Gm. of sodium barbiturate in 100 ml. of distilled water). This buffered F-2 suspension may be stored in a refrigerator for one or two months. Before use, it should be cleared by centrifugation at 3,000 rpm for 10 minutes in order to remove all particulate matter; otherwise, the latter might simulate flocculation.

Preparation of Sensitized Bentonite Particles.—Thoroughly shake the stock bentonite suspension to distribute the bentonite particles evenly. Remove 10 ml. of the uniformly dispersed particles, place in a 15-by-200-mm. culture tube, and centrifuge at 3,000 rpm for five minutes.

Decant the supernatant and add 1 ml. of distilled water to the sediment. Agitate the tube to resuspend the bentonite particles in the 1 ml. of distilled water.

Add 2 ml. of stock F-2 solution and mix gently by tilting and rotating. Allow the suspension to stand from 15 to 30 minutes at room temperature to permit adsorption. Add 15 ml. of distilled water and again mix gently.

Centrifuge for five minutes at 3,000 rpm. Decant the supernatant. Resuspend the sediment with 5 ml. of distilled water, shaking thoroughly. Add another 10 ml. of distilled water, and shake.

Centrifuge as previously. Decant the supernatant, and again resuspend the sediment in 5 ml. of distilled water. Shake vigorously. To this suspension add 1 ml. of 0.1% methylene blue dye; shake, and, after five minutes, add 10 ml. of distilled water and centrifuge.

Decant the supernatant, resuspend the sediment in 10 ml. of distilled water, and centrifuge. Again decant the final washing, and to the sediment add 4 ml. of 0.05 M phosphate buffer, pH 7.3 (made by dissolving 0.975 Gm. of sodium phosphate and 0.185 Gm. of potassium dihydrophosphate in 100 ml. of distilled water). This constitutes the sensitized bentonite particles. Add 0.1 ml. of 1% polysorbate 80 (Tween 80).

Conducting the Test.—The serum to be tested should be inactivated for 30 minutes at 56 C prior to use. Microscopic slides (3 in. by 2 in.) with 12 rings, designed for serologic flocculation tests, are used to conduct the test. In each ring on the slide is placed 0.1 ml. of serial twofold dilutions of serum in phosphate-buffered saline solution at pH 7.4. One drop of sensitized bentonite suspension is added to each ring. (Prior to use, the suspension should be thoroughly shaken.) The drop is of such size that a capillary pipet should dispense about 40 drops per milliliter. The slide is then rotated on a Boerner type of rotating machine at 100 to 120 rpm for 20 minutes and read immediately under a microscope at low-power magnification (60×). Drying is to be avoided.

Reading of Results.—A reaction is regarded as 4+ when all of the sensitized particles are clumped in separate masses. There may be a few large or a number of small clumps, depending on the titer of the serum. Nevertheless, the fields between the flocculi are almost clear. A reaction is regarded as 3+ when approximately three-fourths of the sensitized particles have clumped. A 2+ reaction is one in which half of the particles are clumped and half still remain in colloidal suspension. In a 1+ reaction only one-fourth of the bentonite particles are clumped. In a negative reaction the sensitized bentonite particles are in colloidal suspension. The result of the flocculation test is considered positive when a 2+ or stronger clumping occurs in a serum dilution of 1:32 or higher. Although a negative-reacting serum does not cause any clumping in dilutions up to about 1:1,000, occasionally a 1+ or 2+ flocculation may occur in dilutions of 1:1,000 or higher.

With each test performed, serial saline dilutions of a known positive and a known negative reacting serum should be included in order to detect any change in the sensitized bentonite particles. If debris has gotten into the sensitized bentonite mixture or the control negative reacting serum, false clumping may result. With experience, the spurious aggregates can readily be distinguished from true flocculation. When the result of the test is positive, the flocculi are of uniform density, evenly distributed in the microscopic field, and free of "hyaline-like" material or other debris.

Heating of Serum and Storage Conditions

Necessity for Heating Serum Prior to Testing.—In an attempt to further decrease the time involved in performing the BFT; we studied the need for heating the serum before testing. One hundred tests were simultaneously performed on serum heated to 56 C for 30 minutes and on unheated serum. The effects of heating were found to be significant both in serums with a low titer and in those with moderate and high titers, although the effects were different in these two types. In serum that yielded a positive but low titer (e. g., 1:32 or 1:64) after heating, the reaction was absent; a negative result was obtained when the unheated serums were tested. In some unheated serums with moderate or high titers, again there was no flocculation at all in the first few tubes ("prozone-like" phenomenon), but significant flocculation occurred even in dilutions that extended several tubes beyond the end point obtained when the same serums were tested after heating (table 1). From these observations it is apparent that heating of the serum prior to testing is necessary.

Effect of Serum Storage Conditions on BFT.—The effect of storage of serum under various conditions was also determined. Serum specimens were divided into several aliquots which were then stored at room, refrigerator, and freezer temperatures and tested repeatedly at intervals for six weeks. As indicated in table 2, the titers increased fairly consistently, though slightly, with storage. In rare instances, a negative or "doubtful" result (i. e., 2+ or 3+ flocculation in dilutions of 1:16) obtained with fresh serum became positive after storage (case 5, table 2). A possible explanation for increase in activity of serum on storage is that the rheumatoid factor which had combined with the patient's own gamma globulin in vivo dissociated on storage, making available more "reactive sites" on the rheumatoid factor. These sites are then exposed to the gamma-globulin-coated bentonite, and flocculation results.

Table 1.—*Effect of Heating Serum* on Results of Bentonite Flocculation Test in Two Patients with Rheumatoid Arthritis*

	Case			
	1		2	
Dilution	Heated	Unheated	Heated	Unheated
1:4	++++	−	++++	−
1:8	++++	−	+++	−
1:16	++++	−	+++	−
1:32	++++	+	+++	±
1:64	++++	+++	++	±
1:128	+++	+++	±	+
1:256	+++	+++	−	±
1:512	+++	+++	−	−
1:1,024	++	+++	...	...
1:2,048	+	++	...	...
1:4,096	+	+	...	...

* 56 C for 30 minutes.

Ten serums containing moderate to high titers of rheumatoid factor were stored at −20 C and retested after six months (table 3). Although there was some loss of activity in three of the serums, only one showed negative results. Fourteen with negative findings continued to have negative findings on retesting after storage.

Modifications of the Procedure

Attempts to modify the BFT by simultaneously combining bentonite particles, gamma globulin, and patient's serum on a slide failed to produce a positive reaction. The bentonite particles must be coated prior to their addition to serum.

Occasionally, inactive preparations of pooled human gamma globulin are received. In agreement with the experience of others, it was found that solutions of these inactive preparations could be converted into satisfactory coating agents by heating at 63 C for 10 minutes. Attempts to use commercial preparations of bovine and porcine gamma globulin instead of human gamma globulin were unsuccessful. Bentonite particles coated with these preparations reacted weakly, if at all, with known positive rheumatoid serums. Heating the bovine and porcine gamma globulin at 63 C prior to coating bentonite failed to increase its reactivity. Rheins and co-workers [6] have demonstrated that preparations of gamma globulin from several animal species were suitable "antigens" in the latex-fixation test.

Table 2.—*Effect of Storage on Results of Bentonite Flocculation Test**

		Titers During Storage Time											
		1 Wk.			2 Wk.			4 Wk.			6 Wk.		
Case	Fresh Serum	25 C	5 C	−20 C	25 C	5 C	−20 C	25 C	5 C	−20 C	25 C	5 C	−20 C
3	1:256	1:1,024	1:512	1:256	1:512	1:256	1:256	1:512	1:2,048	1:512	...	1:4,096	1:2,048
4	1:1,024	1:8,192	1:1,024	1:4,096	1:2,048	1:1,024	1:1,024	1:8,192	1:8,192	1:8,192	...	1:2,048	1:4,096
5	Neg.	1:64	1:128	1:512	Neg.	1:128	1:64	1:64	1:64	1:128	...	1:256	1:128
6	1:32	1:128	1:128	1:64	1:64	1:64	1:256	1:32	1:64	1:64	...	1:128	1:128

* Sterile handling of serum was not attempted, and no preservatives were added; in general, there was no gross evidence of bacterial contamination.

Efforts at a further simplification of the BFT produced a slide screening test of equal or slightly greater sensitivity than the original procedure. This modification consists of the addition of one drop of coated bentonite particles to one drop of undiluted, heated serum on a glass slide. The mixture is stirred thoroughly and flocculation directly observed after five minutes. Microscopic examination is helpful in confirming the gross observations and in differentiating bentonite flocculi from debris. Gamma globulin used as a coating agent in this test is routinely heated to 63 C for 10 minutes; the new method eliminates the need for serial serum dilutions, the Boerner type of rotating machine, and special serologic slides.

Table 3.—*Effect of Six Months' Storage at −20 C on Positive Findings*

	Titer After Storage	
Case	1 Wk.	6 Mo.
7	1:8,192	1:8,192
8	1:8,192	1:8,192
9	1:1,024	1:2,048
10	1:1,024	1:1,024
11	1:512	1:512
12	1:256	1:1,024
13	1:128	1:128
14	1:1,024	1:128
15	1:1,024	1:128
16	1:256	Neg.

Table 4 presents the results of a comparison between the BFT and the screening test modification. One hundred forty-four serums from 36 patients with rheumatoid arthritis and 87 from 61 controls were tested.

A disproportionately large number of serums giving doubtful and also false-positive reactions were selected for this analysis. There was agreement of the results obtained by the two tests in 98.2% of serums examined. The BFT doubtful category is considered separately; the result of the screening test was positive in seven and negative in four serums obtained from patients with verified rheumatoid arthritis. In the control series findings in both tests were positive in seven; the screening test detected two additional false-positive results. These two serums were from patients with leukemia. In summary, the result of the BFT was positive in 67% of specially selected cases of rheumatoid arthritis, whereas the slide screening test was positive in 77%. In the controls, a false-positive reaction was obtained in 6% with the BFT and in 10% with the screening test.

Test Results

In order to evaluate the diagnostic usefulness of the bentonite flocculation test only patients whose clinical diagnosis was verified by us were accepted for study. The results of our experience to date with the BFT are presented in table 5. Of 114 patients with verified rheumatoid arthritis, the test finding was positive in 85%. In eight with definite juvenile rheumatoid arthritis there was one positive reaction. This patient has had arthritis since the age of 8 and has active disease at the age of 46. Disseminated lupus erythematosus and scleroderma contributed the next highest percentage of positive tests, 55% and 50% respectively. In 58 patients with nonrheumatoid arthritis, the test finding was positive in 3 (5%).

TABLE 4.—*Comparison of Bentonite Flocculation Test and Screening Modification in Patients with Rheumatoid Arthritis and in Controls*

	Patients		Controls	
Test Result	Total No.	Serums, No.	Total No.	Serums, No.
Positive BFT, positive screening test	23	109	4	7
Positive BFT, negative screening test	1	1	...	...
Negative BFT, positive screening test	1	2	1	1
Negative BFT, negative screening test	5	21	55	78
Doubtful BFT,* positive screening test	4	7	1	1
Doubtful BFT,* negative screening test	1	1	...	...

* Less than 50% of bentonite particles flocculated in serum diluted 1:32.

In our experience, some BFT-negative serums from patients with definite rheumatoid arthritis yielded positive results when the euglobulin fraction of the serum was tested. Euglobulin fractions were prepared by diluting serum in 14 volumes of cold distilled water. After two hours at 5 C, the resulting precipitate was redissolved in buffered saline solution and tested. Six whole serums from patients with rheumatoid arthritis gave negative BFT results; euglobulin preparations from three of these patients were positive in titers of 1:128, 1:256, and 1:512.

Four of 27 patients with leukemia and lymphomas had positive findings (table 5). It is suspected, but not yet proved, that among the abnormal serum proteins produced in these diseases there may be present a macroglobulin which resembles the rheumatoid factor in its ability to react with human gamma globulin. Three of 31 patients with uveitis had positive results. One of these had a brain tumor and macroglobulinemia. The other two patients had no significant history and exhibited no clinical signs or roentgenologic evidence of rheumatoid arthritis.

Among 151 male blood donors in the age group 20 to 45 years were two positive reactors. The incidence of positive reactors among healthy individuals has generally been found to be about 2 to 3%.[7] The BFT result was uniformly negative in 25 normal volunteers.

Variation in BFT Titer.—Although a direct correlation has been found between the full development of rheumatoid arthritis and incidence of positive serologic findings,[1] we have observed in some patients with fully developed rheumatoid arthritis conversion of positive to negative test reactions and the reverse. Repeated bentonite flocculation tests were done at weekly or monthly intervals for periods of four weeks to 10 months in 40 patients with chronically active rheumatoid arthritis. Twenty-six patients had consistently positive results and seven consistently negative results. However, in seven other patients findings were negative and positive at various times. The cause of this inconsistency is unknown; it does not appear to be related to changes in activity of the disease or in the host's response to disease. At any rate, this phe-

TABLE 5.—*Results of Bentonite Flocculation Tests*

Diagnosis	Cases, No.	Positive, No.	Negative, No.
Rheumatoid arthritis			
Adult	114	97(85%)	17
Juvenile	8	1(12%)	7
Collagen disease			
Systemic lupus erythematosus	11	6(55%)	5
Scleroderma	10	5(50%)	5
Dermatomyositis	3	...	3
Nonrheumatoid arthritis			
Rheumatic fever	1	...	1
Rheumatic heart disease (active and inactive)	10	...	10
Gout	24	1	23
Osteoarthritis	13	...	13
Reiter's syndrome	8	1	7
Ankylosing spondylitis (with and without peripheral joint involvement)	5	1	4
Total	61	3(5%)	58
Nonrheumatic disease			
Carcinoma of various organs	45	...	45
Leukemia and lymphoma	27	4	23
Uveitis	31	3	28
Hypercholesteremia	5	...	5
Cirrhosis, alcoholic	5	...	5
Undiagnosed disease	5	...	5
Multiple myeloma	4	...	4
Congenital heart disease	4	...	4
Muscular dystrophy	4	...	4
Osteoporosis	4	...	4
Arteriosclerotic heart disease	4	...	4
Mental defective	3	...	3
Stomatitis	3	...	3
Agammaglobulinemia (with and without arthritis)	3	...	3
Hypothyroidism	3	...	3
Viral infections	3	...	3
Diabetes mellitus	2	...	2
Pseudohermaphroditism	2	...	2
Actinomycosis	2	...	2
Hyperthyroidism	2	...	2
Miscellaneous	31	...	31
Total	192	7(4%)	185
Normal volunteers	25	...	25
Professional blood donors	151	2(1%)	149
Total	176	2(1%)	174
Total controls and normal persons	429	12(3%)	417

nomenon underscores the importance of doing repeated serologic examinations in patients who appear to have rheumatoid arthritis but whose test results are negative on one or more occasions.

Figure 2 illustrates the three types of serial reactions, namely, consistently negative (*top*), intermittently positive and negative (*center*), and consistently positive (*bottom*). All three patients had typical, chronically active rheumatoid arthritis. The disease had been present for 14, 9, and 7 years respectively. Multiple, symmetrical joint involvement and x-ray evidence of cartilage and bone erosion were present. All three patients have received steroid therapy daily, uninterruptedly, for the past four years. There has been sufficient suppression of disease to permit usual activities with minimal to moderate discomfort.

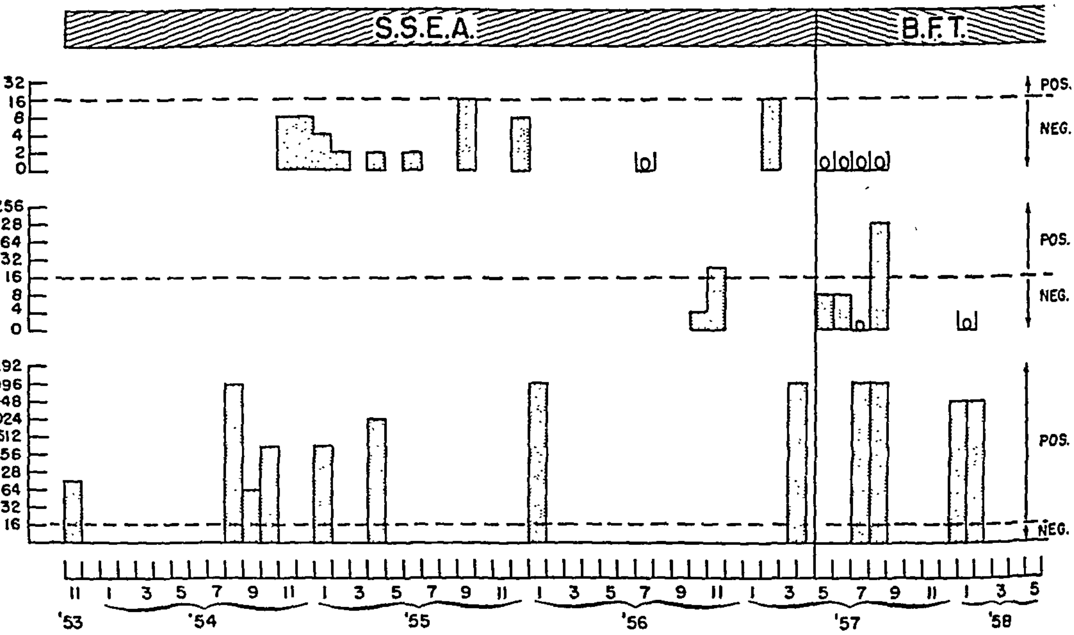

Fig. 2.—Variation in titer of rheumatoid factor in serum of three patients with rheumatoid arthritis: *top*, consistently negative, *center*, intermittently negative and positive, and, *bottom*, consistently positive. (S.S.E.A.=sensitized sheep erythrocyte agglutination test, replaced by BFT in this laboratory in May, 1957.)

Independence of Host Response and BFT.—Although many abnormal laboratory findings in rheumatoid arthritis are restored toward or to normal values after improvement with corticosteroid administration, the positive serologic test for this disease is generally unaltered by therapy. The patient whose case is illustrated in figure 3 was studied during an exacerbation of arthritis induced by reduction in required dosage of steroid. He was a 47-year-old male who had had severe rheumatoid arthritis for eight years. The marked flare of his arthritis was associated with a rise in erythrocyte sedimentation rate and increase in jewelers' ring size (an index of proximal interphalangeal joint swelling). Despite these changes the BFT remained fairly constant; the titer varying by only one tube, 1:256 to 1:512. This case illustrates the dissociation between host response and the serologic reaction.

Comparison of Tests and Effect of Other Serum Macroglobulins

Comparison of BFT and Latex-Fixation Tests.—*In a previous publication,*[7] results obtained by the BFT and sensitized sheep erythrocyte agglutination (SSEA) test done on the same serum samples from 64 patients were compared. There was agreement between results of both tests in 63 samples and disagreement in 1. A similar comparison between the BFT and latex-fixation test was done in this study. The latex-fixation test was carried out according to method of Singer and Plotz.[8] Polystyrene latex particles 0.81 μ in diameter and glycine-buffered saline solutions, pH 8.2, were used.

In 49 patients with rheumatoid arthritis there was agreement of results by both tests in 96% of the serums examined. In two patients with definite rheumatoid arthritis both findings on tests were negative. In the remaining two, the latex-fixation test results were negative and the BFT results positive at titers 1:32 and 1:64. In the nonrheumatoid group, with 58 subjects, again there was agreement between the two tests in 96%. In 55, results of both were negative. In one patient with a definite diagnosis of gout, the results of both tests were persistently positive. Findings in another patient, with syphilis, were negative in the latext-fixation test and positive in the BFT at 1:32. The remaining patient, with cirrhosis, had negative findings in the BFT and positive in the latex-fixation test.

The basic principle of the latex-fixation test and bentonite flocculation test is similar. In both, inert particles are used and pooled human gamma globulin is used to coat or "sensitize" the particles.

Effect of Other Serum Macroglobulins on BFT.—Franklin and associates[9] have described the physical properties of the rheumatoid factor as determined by ultracentrifugation. They have demonstrated a protein of unusual, high molecular weight in about one-third of the serum samples from 31 patients with rheumatoid arthritis. This protein appears to be a circulating complex composed of a macroglobulin (the rheumatoid factor) and one or more gamma globulins of low molecular weight. Electrophoretically, this macroglobulin travels with the faster-moving gamma globulins. A number of other serum proteins share these characteristics of high molecular weight (about one million or more) and gamma electrophoretic mobility. Among these are the macroglobulins responsible for the Wassermann and biological false-positive reactions, some isoagglutinins, the complete Rh agglutinins, cold agglutinins, and macroglobulins and macrocryoglobulins associated with the disease macroglobulinemia of Waldenström.

Rheins and co-workers[10] have reported positive findings in latex-fixation tests in 7 of 24 patients with syphilis. The BFT was performed on serum samples from 25 patients who had positive slide flocculation or complement fixation test findings for syphilis. In two of these patients the BFT results were positive in titers of 1:64.

Serum from 20 patients with positive findings in serologic tests for syphilis, in whom the absence of a history or other evidence of infection suggested a biological false-positive reaction, were examined. Two of these samples gave positive BFT findings in titers of 1:1,024 and 1:2,048. Information indicates that these patients do not have rheumatoid arthritis at present. Moore[11] found that the biological false-positive reactions may precede by many years, or occur concurrently with, rheumatoid arthritis, systemic lupus erythematosus, or "collagen vascular disease." In a group of 68 patients who chronically had biological false-positive reactions, eight had rheumatoid arthritis. It will, therefore, be of interest to determine whether the two patients with positive findings in the BFT will eventually develop rheumatoid arthritis.

Eight serum samples that showed low titers of cold agglutinins have been tested. In one of these a borderline positive BFT finding was obtained.

Macroglobulinemia of Waldenström is characterized by hypergammaglobulinemia,[12] and, on ultracentrifugation, serum from such patients reveals a marked increase in proteins with high molecular weight (sedimentation constant of about 19, as well as lesser amounts of even heavier proteins). The BFT was performed on the serum of four such patients. In two patients a titer of 1:8,192 and 1:16,394 was obtained. In the remaining two patients the BFT result on whole serum was negative. Euglobulin fractions prepared from these serums yielded a positive BFT finding in one.

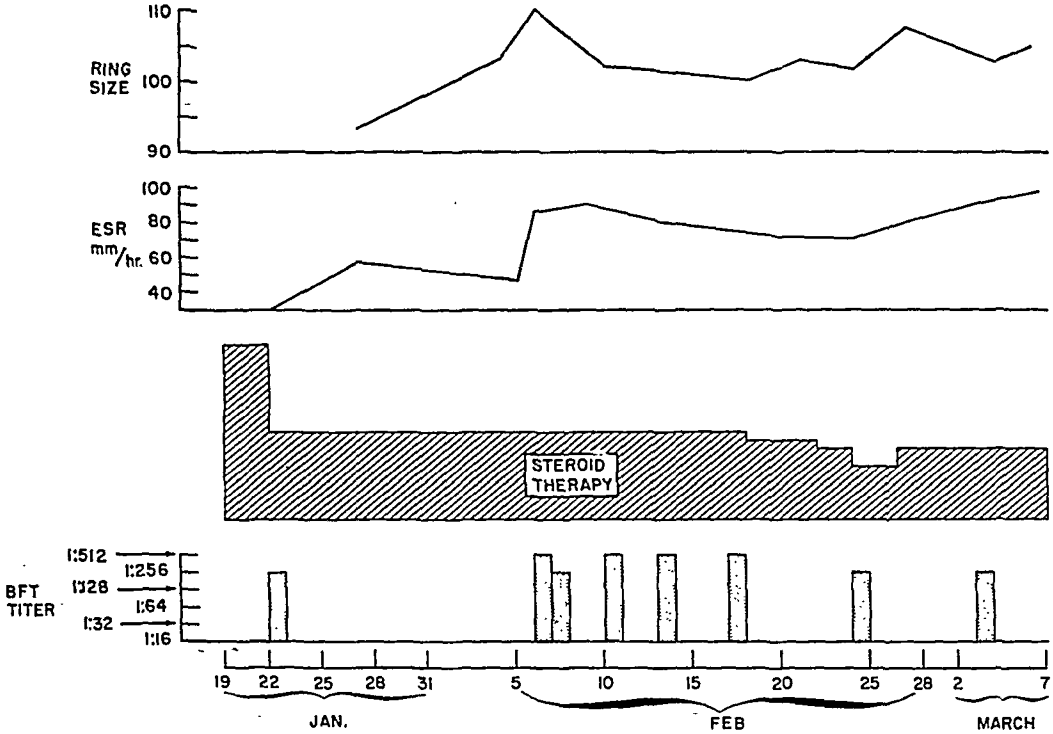

Fig. 3.—Clinical and laboratory recrudescence induced by reduction in steroid dosage (from 30 to 15 mg. of prednisone daily). Effect on swelling of interphalangeal joints (ring size) and erythrocyte sedimentation rate is shown. BFT titer remained independent of patient's clinical condition.

Comment

Serologic testing for rheumatoid factor or factors has been greatly facilitated by the substitution of inert particles for erythrocytes. The substitution of latex or bentonite particles has eliminated the need for absorption of heterophil antibodies and for anti-erythrocyte rabbit serum. Sheep erythrocytes, the most commonly used "carrier" in these tests, vary in behavior at different times of the year and deteriorate on storage. Furthermore, sheep red blood cells coated with rabbit antibody (rabbit gamma globulin) to sheep erythrocytes do not seem to react as sensitively with the rheumatoid factor as cells or particles coated with human gamma globulin. In general, serologic tests with human gamma globulin yield a greater percentage of positive results than do those with rabbit amboceptor.[13] Attempts to use bovine and porcine gamma globulin as coating agents in the BFT were unsuccessful.

In sheep cell agglutination reactions, it is necessary to heat the test serum to 56 C for 30 minutes in order to destroy components of complement and thereby avoid hemolysis. Even in the BFT, in which erythrocytes are not used, it was also necessary to heat the serum. Singer,[14] as well as others, has demonstrated that no fraction of complement plays a role in either sensitized sheep cell or latex-fixation reactions. Heating of serum, however, in addition to inactivating complement, denatures proteins. Electromigration of canine serum was markedly affected by such treatment; serum proteins migrated faster than those in the unheated controls.[15] The existence of a complex composed of rheumatoid factor and the patient's own gamma globulin has been mentioned previously. Rheumatoid factor may be undetectable because it is "bound" to the patient's gamma globulin. Mild heating of the serum may denature gamma globulins or otherwise disrupt the complex and thus make rheumatoid factor available for reactions with the test system.

The BFT result is positive in about 10% of syphilitic as well as biological false-positive serums. Peltier and Christian[16] found a similar incidence of positive results in F-2 coated, tanned sheep cell tests in a large series of syphilitic serum samples. Positive BFT results were obtained in three of four patients with Waldenström's macroglobulinemia. It is noteworthy that in both tests human gamma globulin is employed. These results suggest that one may expect false-positive results in serologic tests for rheumatoid arthritis in diseases in which macroglobulins are produced. It remains to be determined whether the property of reacting with gamma globulin is characteristic of a species of molecules, i. e., macroglobulins, or only of one member of the species, i. e., rheumatoid factor. The occurrence of positive findings in tests for rheumatoid arthritis in a variety of nonarthritic diseases does not detract from the value of the tests as laboratory aids in the differential diagnosis of polyarthritis.

Summary

The bentonite flocculation test and the screening test modification are simple, reliable, and sensitive laboratory aids in the diagnosis of rheumatoid arthritis. Positive test results were obtained in about 85% of verified cases of rheumatoid arthritis. The incidence of false-positive results in 429 controls was 3%. Diseases in which macroglobulins are produced may give 10% or more false-positive results in serologic testing for rheumatoid arthritis.

We are indebted to Mr. Ad Harris, Venereal Disease Research Laboratory, Chamblee, Ga., for supplying biological false-positive serums.

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BENTONITE FLOCCULATION TEST IN RHEUMATOID ARTHRITIS

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The bentonite flocculation test was applied to the serums of 48 patients who satisfied all the clinical criteria for rheumatoid arthritis. Positive results were obtained in 40 and false-negatives in 8 (17%). Of 12 patients with the probable diagnosis of rheumatoid arthritis, 4 gave positive results, and 8 (67%) gave false negatives. The test was also applied in other rheumatic conditions, with negative results in 17 out of 19 cases of rheumatoid spondylitis and negative results in all of 15 cases of osteoarthritis with fibrositis, indicating that these two conditions differ significantly from rheumatoid arthritis. Applied to 68 other patients with symptoms involving the joints, the test gave negative results in all but four (2 out of 10 patients with gout, 1 out of 4 with lupus erythematosus, and 1 out of 12 with essential hypertension). The bentonite flocculation test is comparatively simple and inexpensive, and these data indicate that it is a useful laboratory aid in the diagnosis of rheumatoid arthritis.

The clinical diagnosis of a disease entity deserves, in most instances, its corroboration by specific laboratory findings. This is especially true when the symptoms and signs of an illness may simulate other conditions. In the field of rheumatic diseases, this is a frequent occurrence. An indication that the proper diagnosis of rheumatoid arthritis in clinical practice is not as simple or as frequently made as is generally believed is demonstrated by the necessity for the development of diagnostic criteria by the American Rheumatism Association.[1] Therefore, a laboratory test which will aid in establishing a diagnosis of rheumatoid arthritis by either corroborating an obvious clinical impression or reassuring a doubtful one is desirable. The test should be accurate, with as few false-positive and negative results as possible; simple, not requiring highly trained personnel to perform it; and inexpensive, so that it can be used without creating an economic burden on the patient or the institution.

Since 1930, when Cecil and co-workers[2] reported on the agglutination of certain strains of streptococci by serum from patients with rheumatoid arthritis, considerable work has been done both in the search for a diagnostic test that will fulfill these criteria and in the identification of the factor or factors responsible for these reactions. In 1940, Waaler[3] demonstrated the capacity of serum from patients with rheumatoid arthritis to agglutinate sensitized red blood cells, and in 1948 Rose and associates[4] stimulated additional interest in the hemagglutination reactions by introducing the differential agglutination test. In 1954 Heller and co-workers[5] detected a substance in human blood fraction 2, the gamma globulin fraction, which had a great affinity for the factor or factors present in the serum of patients with rheumatoid arthritis, paving the way for the development of simpler serologic tests. With use of some other particulate matter and fraction 2 as the sensitizing substance, the necessity for either absorbing the heterophylic antibodies or having to perform differential hemagglutination tests, both of which are intricate and time consuming, was obviated. Work toward this end was initiated by Plotz and Singer[6] when they introduced the use of polystyrene latex particles. The accuracy and relative simplicity of this test have been recently corroborated by Rothermich and Philips.[7]

At the Ninth International Congress on Rheumatic Diseases at Toronto, Canada, in June, 1957, Bozicevich and associates[8] reported on the use of bentonite particles in a flocculation test for rheumatoid arthritis. This test appeared to be equally accurate, as simple to perform, and a more economical procedure than the tests previously devised. These reports stimulated us to investigate the bentonite flocculation test for use in our patients.

Methods

The bentonite flocculation test was performed as described by Bozicevich and associates.[9] A suspension of bentonite particles of a specific size, those obtained by centrifugation at 1,300 to 1,600 rpm, will not tend to flocculate spontaneously and will be active for several months when kept at room temperature. A solution of fraction 2, derived from pooled human serum and prepared by dissolving 0.5 Gm. of the dried gamma globulin in 50 ml. of barbital (Veronal) buffer, will maintain its potency for one to two months when stored at 5 C. Sensitization of the bentonite particles is performed as described by Bozicevich and associates.[9] These sensi-

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tized particles remain active for an average of one week when stored in the refrigerator, as demonstrated in table 1. This obviates the need for a fresh preparation every time the test is to be performed.

When an immediate test was not required, it was convenient to store the serum in a frozen state, until two or more tests could be performed at the same time, without variation in results (table 2).

TABLE 1.—*Activity, in Titer of Serum Reaction, of Sensitized Bentonite Particles After Storage*

Case	Storage Period		
	Control	1 Wk.	2 Wk.
1	1:512	1:512	1:4
2	1:512	1:512	1:8
3	1:128	1:256	1:2
4	1:256	1:256	1:8

This experience confirms previous reports [10] that the rheumatoid factor is not altered by storage of the serum in a frozen state. The initial test on these patients was performed on the day of collection, while the retesting was done at varying intervals of time. Titers in both instances were identical, although in some instances there were minor differences in the reaction.

Results

Rheumatoid Arthritis.—The serum of 60 patients with rheumatoid arthritis was tested. The diagnosis was established according to the criteria of the American Rheumatism Association,[1] prior to the performance of the serologic test, and confirmed as such by one of us (R. T. S.). The results are summarized in table 3, along with those for other conditions. Forty-eight of these patients had definite rheumatoid arthritis; 40 (83%) gave positive results in the flocculation test. Twelve patients were classified as probably having rheumatoid arthritis, with 4 (33%) exhibiting positive results.

TABLE 2.—*Reaction of Serum After Storage*

Case	Date of Test	Titer
5	11/13/57 3/ 7/58	1:1,024 1:1,024
6	12/12/57 3/17/58	1:2,048 1:2,048
7	12/16/57 1/1/58	1:512 1:512
8	12/16/57 1/13/58	1:1,024 1:1,024
9	12/20/57 3/ 7/58	1:256 1:256

The duration of illness in both groups was similar, ranging from six months to 30 years. Two patients with rheumatoid arthritis also had gout. The diagnoses of both types of arthritis were established several years prior to the test. In each instance there was a strongly positive serologic reaction.

Sixteen patients with rheumatoid arthritis had negative findings in the bentonite flocculation test. This group deserves further comment. Seven of these patients had definite clinical rheumatoid arthritis; therefore, their reactions are truly false-negative. The remaining nine individuals were classified as probably having rheumatoid arthritis. Two of this latter group had articular involvement limited to the knee joints. A 49-year-old man has had recurrent inflammatory changes in both knees during the past nine years. A synovectomy on the right knee was performed several years ago, with a pathological diagnosis of chronic synovitis. A 37-year-old man had poliomyelitis during adolescence, with neurological residuals involving the right upper and lower extremities. For the past five years he has had recurrent inflammatory joint disease, involving both knees.

TABLE 3.—*Findings on Bentonite Flocculation Test in Patients with Rheumatoid Arthritis, Other Rheumatic Conditions, and Other Illnesses*

Diagnosis	Patients Tested, No.	Reactions, No.	
		Positive	Negative
Rheumatoid arthritis			
Definite	48*	40* (83%)	8
Probable	12	4 (33%)	8
Total	60	44 (73%)	16
Rheumatoid spondylitis	19	2 (11%)	17
Other rheumatic conditions			
Scleroderma	3	...	3
Systemic lupus erythematosus	4	1	3
Osteoarthritis and fibrositis	15	...	15
Gout	10*	2*	8
Allergic vasculitis and arthritis	1	...	1
Postcommissurotomy syndrome	1	...	1
Active rheumatic heart disease	1	...	1
Total	35	3	32
Other illnesses			
Acute hepatitis and Laennec's cirrhosis	9	...	9
Acute glomerulonephritis	2	...	2
Infectious mononucleosis	2†	...	2
Recent streptococcic infection	6‡	...	6
Suspected syphilis	17§	...	17
Essential hypertension	12	1‖	11
Total	48	1	47

* Includes two patients with combined rheumatoid and gouty arthritis.

† Heterophil antibody titer, 1:896 and 1:1,793.

‡ Rheumatic fever or acute glomerulonephritis. Antistreptococci units given: 50, 100, 12, 125, 166, and 2,500.

§ Twelve with negative and 5 with positive findings in Venerea Disease Research Laboratory tests.

‖ Bentonite flocculation test titer: 1:2,048.

The remaining seven patients had minimal inflammatory joint changes of a chronic nature involving, in most cases, only a few joints. All had a normal hemoglobin level, but some had an elevated sedimentation rate. Five, however, received therapy with gold salts and/or steroids at one time or another. These six patients most probably had a low-grade type of rheumatoid arthritis.

Rheumatoid Spondylitis.—The serum of 19 patients with rheumatoid spondylitis was tested. The diagnosis was reconfirmed prior to the performance of the test and was based on clinical and x-ray findings. Most of these patients also had peripheral joint involvement. However, in all of them, the initial episode was that of spondylitis, the peripheral manifestations occurring later. Only two individuals had a positive result in the bentonite flocculation test, and only in a titer of 1:32. Fourteen of these patients had a titer of 0. This, in our opinion, is further evidence that rheumatoid arthritis and rheumatoid spondylitis, even when followed by peripheral joint manifestations, are probably two distinct clinical entities.

Other Rheumatic Conditions.—The serum of 35 patients with other rheumatic diseases, conditions in which the diagnosis is often confused with rheumatoid arthritis was tested. These results are also summarized in table 3. Thirty-two members of this group had negative findings, and three had positive reactions. Two of the patients with a positive result had coexistent gouty and rheumatoid arthritis and have been reported on previously. The other patient had hemolytic anemia and multiple systemic disease, considered to be systemic lupus erythematosus, and at autopsy was also found to have homologous serum jaundice.

Other Illnesses.—A group of patients was selected from the medical ward and clinics of the Pennsylvania Hospital, who, because of the nature of their illnesses, could conceivably have abnormal protein or antibody production and consequently be more likely to exhibit a false-positive reaction in the bentonite flocculation test (table 3). Only 1 of these 48 patients had a positive result. This patient is being followed up at the Hypertension Clinic. At the present time, there is no evidence of an active or incipient rheumatoid arthritis.

Of patients with liver disease, 16% have been previously reported to give false-positive results in serologic tests for rheumatoid arthritis.[11] None of nine patients with either chronic or acute liver disease, one of whom was in hepatic coma, gave a positive result in the bentonite flocculation test.

Summary and Conclusions

A total of 160 patients' serums have been subjected to the bentonite flocculation test. The test is easier and less expensive to perform than any of the heretofore described serologic tests for rheumatoid arthritis.

Eighty-three per cent of 48 patients with definite rheumatoid arthritis and 33% of 12 with probable rheumatoid arthritis had positive findings in the flocculation test. These results are comparable to those in previously reported serologic tests with more difficult and expensive procedures.

Only 2 of 19 patients with rheumatoid spondylitis had positive results, and only in the lowest positive titer, although the majority of these patients have subsequently developed peripheral joint involvement. This, again, stresses that these two conditions probably have different etiologies.

Only 3 of 35 patients with other rheumatic conditions exhibited positive results, and 2 of these had had previous diagnosis of combined gouty and rheumatoid disease. Only one, then, a patient with systemic lupus erythematosus, had a true false-positive reaction. Previous reports stated that 20 to 30% of patients with this condition will give false-positive reactions to serologic testing for rheumatoid arthritis, suggesting a possible relationship between the two conditions.

Of 48 hospital and clinic patients comprising a heterogeneous group of conditions characterized by altered protein metabolism, only one gave a positive result. This patient had a mild type of hypertension with no evidence of a rheumatoid state, but further studies and observations are indicated.

This report substantiates the conclusion that the bentonite flocculation test is the most recent, useful advance in rheumatoid serology and is an additional step toward the development of an accurate, simple, inexpensive, and dependable laboratory aid for the diagnosis of rheumatoid arthritis.

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EXTRAHEPATIC COMPLICATIONS ASSOCIATED WITH CIRRHOSIS OF THE LIVER

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The treatment and prognosis of alcoholic cirrhosis of the liver must take into account the possibility of coexistent disease in other organs. The frequency of extrahepatic disease was studied in the histories of 201 patients in whom the diagnosis had been established by the anamnesis of chronic alcoholism and (in 55 cases) by examination of tissues. The diseases most frequently found were chronic lung disease, diabetes mellitus, peptic ulcer, and cholelithiasis (32, 19, 17, and 17 cases respectively). The symptoms associated with cirrhosis in the 201 patients were spider angioma, ascites, palpable spleen, and hematemesis in 55%, 52%, 27%, and 15% respectively. Although there is disagreement as to the significance of some of these associations, they suggest that the patient with alcoholic cirrhosis has an increased tendency to develop extrahepatic disease.

Our investigation into the problem of chronic alcoholism has included clinical studies of the patients who have developed alcoholic cirrhosis of the liver (Laennec's cirrhosis). In addition to the usual complications of hepatic decompensation and portal hypertension, the occurrence of extrahepatic disease has frequently modified management and prognosis of these patients. This study surveys these diseases occurring outside the liver.

Methods

The clinical records of 201 patients with alcoholic cirrhosis of the liver were analyzed. These cases were found by evaluating the records of the 574 patients who had a diagnosis of cirrhosis made in the University Hospital during the years 1950 to 1955. Only the records of patients with a history of chronic alcoholism and evidence of cirrhosis were utilized in this study. A tissue diagnosis of portal cirrhosis was established in 55 of the 201 patients, 24 by liver biopsy and 31 by autopsy. Three of the autopsied patients displayed a combination of alcoholic and postnecrotic cirrhosis. Those patients with a tissue diagnosis of only fatty infiltration of the liver were excluded from this study.

The remaining 146 alcoholic patients were considered to have cirrhosis by objective clinical evidence. These patients had either a sulfobromophthalein retention greater than 15% in 45 minutes or the combination of sulfobromophthalein retention greater than 5% in 45 minutes and the presence of ascites, splenomegaly, or esophageal varices. If these abnormalities could be reasonably explained on some other basis, e. g., congestive heart failure or extrahepatic biliary obstruction, the case was excluded from the study unless additional evidence in favor of cirrhosis was present, e. g., spider angioma (hemangioma) or typical serum protein level abnormalities. In this clinical group, of course, we often could not rule out other types of cirrhosis or simple fatty infiltration of the liver.

Of the 574 patients considered to have cirrhosis, 373 were excluded from this study for several reasons: 198 patients had insufficient or equivocal evidence of cirrhosis, 82 were considered to have postnecrotic cirrhosis or portal cirrhosis witho
alcoholism, and 93 had cirrhosis of some other typ
especially biliary and cardiac cirrhosis.

Results

The frequency of various disease states in the 2
patients with alcoholic cirrhosis is given in t
table. Because of the small number of patients i
some categories, percentages have not been i
cluded. In the subsequent paragraphs, for the sa
of simplicity, the "liver biopsy" group of cases h
been combined with the "clinical" group to au
ment the clinical group to 170.

Patients' Statistics.—The ages of the patien
when the diagnosis of cirrhosis was originally e
tablished in this hospital ranged between 24 and
years. Sixty-eight per cent of the patients we
between 40 and 60 years old, the median age bein
50 years. For males, the median age at the tim
of diagnosis was 52 years, while for females it wa
43 years. In the autopsy group the ages at the tim
of death ranged between 41 and 87 years, th
median age being 57 years.

There were 157 males and 44 females. Seven
the males and three of the females were Negro. A

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of the remaining patients were Caucasian. In the autopsy group there were 23 males and 8 females, including one Negro female.

Liver Function Tests.—A series of liver function tests was obtained in most of the patients at the time a diagnosis of cirrhosis was initially considered. Determination of the sulfobromophthalein retention at 45 minutes helped to grade the severity of hepatic dysfunction as mild (less than 15%), moderate (15 to 50%), or severe (more than 50%). Hence, dysfunction was considered mild in 42 cases, moderate in 121 cases, and severe in 38 cases.

Hematemesis.—Thirty-two patients had vomited blood within the preceding three years, generally within the preceding month or during hospitalization. The source of bleeding was ascribed to esophageal varices in 18 patients (with x-ray evidence alone in 11, autopsy proof alone in 5, and combined proof in 2), to duodenal ulcer in 3, to superficial gastritis in 1, and to diffuse gastrointestinal bleeding in 1.

Results of Examination.—Spider angioma, ascites, and a palpable spleen were found in 55%, 52% and 27% of the 201 patients respectively. In the autopsy group these features were found in 65%, 74%, and 32% respectively. Spider angioma was not found in any of the 10 Negro patients.

Esophageal varices were demonstrated in 23 (14%) of the 170 clinical patients and in 19 (61%) of the autopsied patients. Bleeding was ascribed to these varices in 18 of these 42 patients, 11 occurring in the clinical group and 7 in the autopsy group. In 5 of the 19 patients with varices in the latter group, upper gastrointestinal x-rays had been described as normal; in only one of these patients, however, had bleeding occurred. It is also of interest that in these 19 patients with varices, spider angiomas were noted in 16, the 3 exceptions including 1 Negro and 1 moribund patient with an incomplete physical examination; in the 12 autopsied patients without esophageal varices, spider angiomas were noted in only 4.

Upper gastrointestinal x-rays were obtained in 150 of the 201 patients. There were no abnormalities in 101, esophageal varices in 27, hiatus hernia in 11, antral gastritis in 3, and duodenal ulcer in 8. Cholecystograms were obtained in 102 patients. There were no abnormalities in 32, faint visualization in 18, nonvisualization in 42, opaque calculi in 6, nonopaque calculi in 2, and questionable calculi in 2. In the group of 42 patients with nonvisualized gallbladders, 31 studies were done when the patient's sulfobromophthalein retention was greater than 20%.

Diseases Present.—In addition to the total group of 19 patients with established diabetes mellitus, there were 6 patients with either borderline fasting hyperglycemia or mild glycosuria without blood sugar level determination. Blood sugar levels were not measured in 94 patients, but urinalyses were done in all 201 patients. Glucose tolerance tests were not considered diagnostic of diabetes mellitus unless the fasting blood sugar levels were also elevated. One patient was not included because his hyperglycemia coincided with an attack of acute pancreatitis.

The 10 cases of peptic ulcer in the clinical group consisted of one active duodenal ulcer, eight healed duodenal ulcers, and one gastric ulcer. In the autopsy group there were two patients with acute bleeding duodenal ulcer, two with small acute duodenal ulcer, one with chronic duodenal ulcer with perforation, and two with small gastric ulcer. In one patient, the bleeding duodenal ulcer was not recognized before death.

The cholecystogram results have been described above. Two patients had previously had cholecystectomy for gallstones. Most of the gallstones discovered at autopsy had not been suspected clinically. In addition, there were two cases of acute cholecystitis without stones which contributed to the death of two patients in the autopsy group. Another two patients in the autopsy group had chronic cholecystitis without stones; this increased the frequency of gallbladder disease in this group to 11 of 31. These patients included seven males and four females.

Diseases Associated with Alcoholic Cirrhosis

	Basis for Diagnosis of Cirrhosis			
	Clinical	Liver Biopsy	Autopsy	Total
Total no. of patients	146	24	31	201
Diabetes mellitus, no.	12	2	5	19
Peptic ulcer, no.	10	..	7	17
Cholelithiasis, no.	8	2	7	17
Pancreatitis, no.	1	..	3	4
Chronic lung disease, no.	21	1	10	32
Hypertension, no.	12	1	1	14
Congestive heart failure, no.	7	1	1	9
Myocardial infarction, no.	2	..	1	3
Malignant neoplasm, no.	7	2	4	13

Although only one case of pancreatitis was confirmed in the clinical group, two additional patients had histories suggesting recurrent pancreatitis. Many other patients with nonspecific pain in the upper part of the abdomen did not have serum amylase or lipase level determinations. The three cases of acute pancreatitis in the autopsy group had not been suspected clinically. Pain was described in only one of the three patients, and even in this patient it was not emphasized. Nevertheless, the pancreatitis was moderately severe in each case, was superimposed on chronic pancreatitis in two patients, and was accompanied by terminal hepatic coma in two. A serum amylase level was obtained in only one of the three patients; this was on a postmortem specimen and was within normal limits. There was surprisingly no overlap between these three patients and the seven autopsied patients with cholelithiasis.

Most of these patients in both the clinical and autopsy groups had chronic bronchitis with obstructive emphysema, associated with excessive cigarette smoking. The remaining patients had active tuberculosis, chronic pneumonitis of uncertain etiology, bronchial asthma, and bronchiectasis.

There were 14 patients with hypertension, and in each instance the diastolic pressure was greater than 100 mm. Hg. Except for two with chronic nephritis, these patients were considered to have essential hypertension. In only 1 of the 14 patients with hypertension was the diastolic pressure persistently above 120 mm. Hg. Several patients, however, reportedly had had hypertension in the past and were not examined at this hospital until their cirrhosis had become severely decompensated. Three of the patients in the clinical group had had "strokes."

Of the three patients with myocardial infarction, two had typical histories and electrocardiograms of old infarctions. One autopsied patient had a fatal myocardial infarction superimposed on an old infarction. The cirrhosis was severe in only one of the three patients. Three additional patients had angina pectoris; hence, there were six patients in all with coronary artery disease.

In the congestive heart failure group, there were nine patients with cardiac decompensation; two had hypertension, one had aortic insufficiency, and six probably had arteriosclerosis.

The clinical group included nine patients with malignant neoplasms: three of the lungs, two of the cervix, one of the colon, one of the larynx, and one of the tongue; one patient had carcinomatosis of unknown origin. In the autopsy group were one patient with hepatoma, one with carcinoma of the esophagus, one with prostatic carcinoma, and one with malignant degeneration of a rectal polyp—a total of 13 in the two groups.

In regard to other associated diagnoses, there were 13 patients with syphilis (2 with tertiary and 11 with latent), 6 with gout, and 5 with psoriasis. In several patients there was a history suggesting functional hypoglycemia, but this was proved in only one case. Organic hypoglycemia was not established in any patient. There were several patients with chronic renal disease, but acute glomerulonephritis was not observed.

Cause of Death.—Death was ascribed to gastrointestinal hemorrhage in 13 patients, hepatic coma in 8, postoperative shock in 2, peritonitis in 2, pulmonary infarction in 2, myocardial infarction in 1, pneumonia in 1, and acute gastric dilatation in 1. Gastrointestinal hemorrhage was due to esophageal varices in seven, diffuse intestinal bleeding in three, duodenal ulcer in two, and superficial gastritis in one.

Factors contributing to death included pulmonary infarction in two patients, acute pancreatitis in two, acute cholecystitis in two, diverticulitis in two, and various infections in four. Terminal bronchopneumonia and terminal cholemic nephrosis were not tabulated. There were also 15 deaths without autopsy, 8 at this hospital and 7 away from this hospital. The major causes appeared to be hepatic coma, extrahepatic malignancy, and gastrointestinal hemorrhage (in two).

Comment

Some months after we had outlined and instituted our own studies of this problem, MacDonald and Mallory[1] reported a study on the natural history of postnecrotic cirrhosis. Their study included some interesting figures on the incidence of extrahepatic complications in 221 autopsied patients; these diseases were as follows: diabetes mellitus, 4.8%; active pancreatitis, 6%; gastric and duodenal ulcer, 9%; nonhepatic neoplasm, 12%; moderate or severe degree of atherosclerosis and myocardial infarction (six patients), 73%; and primary hepatic carcinoma, 14%.

It has been our impression that the patient with alcoholic cirrhosis has an increased tendency to develop extrahepatic disease. It seems logical that the chronic alcoholism, the altered dietary intake, and the multiple metabolic changes secondary to the hepatic disease should adversely affect tissues and organs throughout the body. To prove this postulate, however, is beyond the scope of this paper. A parallel analysis of an appropriate control group has been unavailable.

A review of the literature reveals considerable disagreement about the significance of certain disease interrelationships. Attempting to associate diabetes mellitus with portal cirrhosis is a good example.[2] Merely establishing the diagnosis of diabetes in the presence of liver disease can be difficult. The glucose tolerance test findings in cirrhosis may simulate those seen in patients with early diabetes. The fatty liver of the obese diabetic person or the enlarged liver of a patient with poorly controlled diabetes may be erroneously interpreted as indicative of cirrhosis. Pancreatitis is more frequent in alcoholics;[3] 10 to 15% of patients with chronic pancreatitis develop frank diabetes mellitus, and probably many more have an impaired glucose tolerance typical of diabetes.[4] Hemochromatosis may erroneously be considered as simple portal cirrhosis with diabetes mellitus.[5] Pancreatic deficiency secondary to Kwashiorkor and other diseases of malnutrition may simulate diabetes.

In our study, 9.5% of the 201 patients had established diabetes mellitus; an additional 3% may possibly have had diabetes, as demonstrated by a borderline glucose tolerance curve.

Referring specifically to the autopsy group, 5 of the 31 autopsied patients had diabetes mellitus (16.1%), 7 had peptic ulcer (22.6%), 11 had cholelithiasis or cholecystitis (35.5%), 3 had pancreatitis (10%), 10 had chronic lung disease (30%), 4 had malignant neoplasms (12.9%), and there were 3 (10%) with hypertension, congestive heart failure, and myocardial infarction.

Summary

An analysis was made of 201 cases of alcoholic cirrhosis of the liver (Laennec's cirrhosis). The disease was proved in 24 patients by liver biopsy, and in an additional 31 by autopsy. Effort was directed toward analyzing disease occurring outside the liver in these patients. Such extrahepatic complications included diabetes mellitus, peptic ulcer, cholelithiasis, pancreatitis, chronic lung disease, cardiovascular disturbances, and malignant neoplasms.

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INTERNAL FIXATION OF THE FIBULA IN FRACTURES OF BOTH BONES OF THE LEG

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In 15 cases of fracture of both bones of the leg, internal fixation of the fibula was carried out as the principal means for splinting the tibia. The effectiveness of this method is explained by the anatomical relationship of these two bones. Eleven of the 15 cases were acute fractures of the supramalleolar region, but the advantages of the operation were also demonstrated in cases of infected nonunion of the tibia, since the area of fracture could be stabilized without disturbing the tibial site. Functional results have generally been gratifying. Internal fixation of the fibula is effective in the following situations: supramalleolar fractures, badly comminuted or compound diaphysial fractures, transcondylar fractures, and fractures with nonunion or malunion.

Although fixation of the fibula as a means of handling fractures of both bones of the leg may be in rather general usage, it is our opinion that its merits have not been sufficiently emphasized. In our experience with a relatively modest number of cases we have been impressed with the advantages of the method and have, for selected cases, adopted it as standard procedure.

In the period from 1952 through 1957, only 15 of a total of 443 fractures of both bones of the leg were treated by members of the orthopedic staff of John Sealy Hospital by means of internal fixation of the fibula. We are thus aware of the limitations of open reduction and fixation of the fibula as a method of treatment, but we are equally aware of the effectiveness of this method among those fractures of both bones of the leg which, because of

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level of involvement or because of degree of comminution or compounding, may not be treated readily or effectively either by conservative means or by internal fixation of the tibia.

The fibula is the natural splint of the tibia. It is firmly bound to the larger bone through the ligaments of one diarthrodial joint, the proximal tibiofibular, and of one syndesmosis, the distal tibiofibular, and through the fibers of the interosseous membrane, this relationship constituting a second syndesmosis (fig. 1). The proximal joint is situated posterolaterally and has an oblique transverse plane with the head of the fibula actually resting partly beneath the lateral condyle. The distal joint has a vertical plane, and the ligaments in this area incline obliquely distally from tibia to fibula as do the principal fibers of the interosseous membrane.[1]

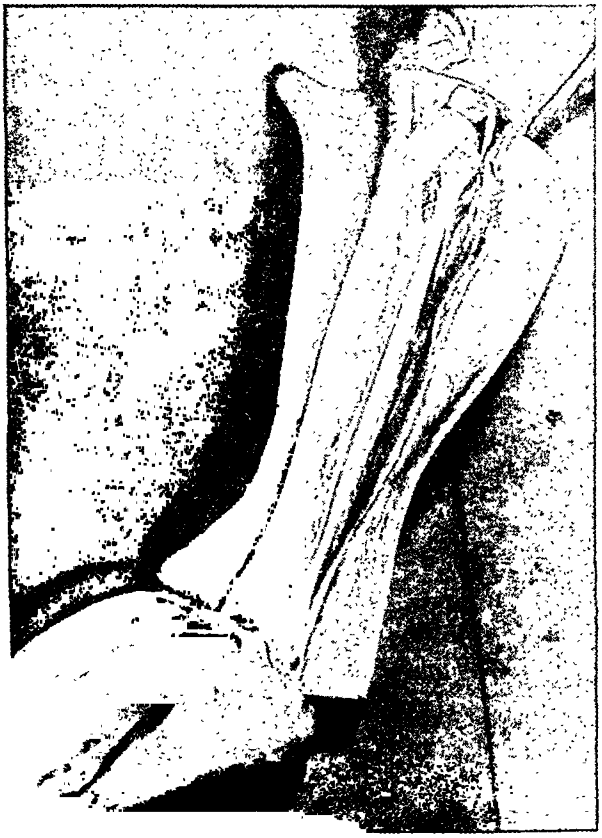

Fig. 1.—Anterior dissection with tibia and fibula freed of overlying musculature, to show proximal and distal joints and interosseous membrane. Inclination of major fibers of interosseous membrane distally from tibia to fibula is evident.

Because of this anatomic arrangement, the tibia is often visualized as a support for the fibula, a non-weight-bearing bone of secondary importance. The fibula, on the other hand, may indeed support the tibia through these same structures as in fractures of the tibia alone. Because it often unites with disconcerting readiness, the fibula may actually assume some of the load of the tibia and will even increase in lateral dimension when there is delay or failure of tibial union. In addition, it should b noted that the ligaments of the two joints ofte remain intact in fractures of both bones, and th tibial fragments are displaced with the fibula. Th interosseous membrane is frequently torn, but, the two joints are intact, reduction of one bone wi tend to realign the other. With these observatio in mind, one may consider as anatomically soun the restoration of fibular continuity in certain dif cult fractures of both bones of the leg.

The concept of utilization of the fibula as t splint of the tibia is an old one. Lane,[2] in 1914, su gested open reduction of the fibula in abductio ankle fractures. Farr,[3] in 1927, mentioned the use open fibular reduction in fractures with badly com pounded or comminuted tibial components. Cam bell,[4] in 1939, proposed open reduction of the fibu for unstable oblique and comminuted fractures the tibia, for stabilization of ununited fractures the tibia, and for bimalleolar fractures.

Of the 15 fractures in our series (table 1), 13 we acute and 2 were nonunions. Of the 13 acute fra tures, 11 were of the supramalleolar area, one the shaft, and one of the upper extreme or tran condylar area of the tibia. Eight of the acute fr tures were of the open variety. Two patients h bilateral supramalleolar fractures. Of the nonunio one was of the lower one-third and one of t supramalleolar region. A third case of failure union, a supramalleolar fracture, was treated by as an acute fracture with fibular fixation and by t same means as a nonunion. Its inclusion as a sep rate fracture would increase to 16 the total numb

Table 1.—*Fractures Treated by Means of Internal Fixat of the Fibula, 1952 through 1957*

Level of Fracture	Acute, No. Open	Acute, No. Closed	Nonunion, No.	To
Supramalleolar	7	4	1	1
Lower one-third	..	..	1	
Diaphysial	1	..	..	
Transcondylar	..	1	..	
Total	8	5	2	1

From the available literature and from our ow experience it is apparent that in fractures of bo bones of the leg fixation of the fibula is occasio ally a useful mode of treatment in (1) ankle fr tures,[5] (2) supramalleolar fractures, (3) severe comminuted or compounded diaphysial fractur (4) transcondylar fractures, and (5) fractures w nonunion or malunion. This list is further qualifi in the sections below, which include only th types of fractures with which we have had perso experience.

Supramalleolar Fractures

Among the most difficult to handle of fractu of both bones of the leg are those involving t supramalleolar region of the tibia. This region h no muscle attachment and thus no protective supportive soft tissue other than the overlying tendons. Fractures occurring at this level tend to be severely comminuted and disorganized because of the lack of soft tissue support, and they are often compounded because of the immediately subcutaneous plane of the tibia anteromedially.

These fractures may be roughly classified as transverse (fig. 2*A* and *B*), resulting from direct trauma; spiral-oblique (fig. 2*C* and *D*), resulting from torsion; and compressed (fig. 2*E* and *F*), resulting from trauma transmitted through the ankle. The transverse fractures are usually strictly supramalleolar in level, being 2 or 3 cm. above the mortise; the spiral-oblique fractures extend into the lower one-third of the tibia. Joint involvement in these two types is not, as a rule, severe. Compression fractures, however, tend to involve the malleoli and to cause severe disruption of the articular surface of the tibia.

Perhaps the more common methods of handling supramalleolar fractures are by means of manipulation and plaster only or by the incorporation in plaster of distracting Steinmann pins through calcaneous and proximal tibia. One may attempt reassemblage of the tibial fragments by the use of multiple transfixation pins or screws, but it is hazardous to disturb from the original clot these fragments, the blood supply of which is at best pre-

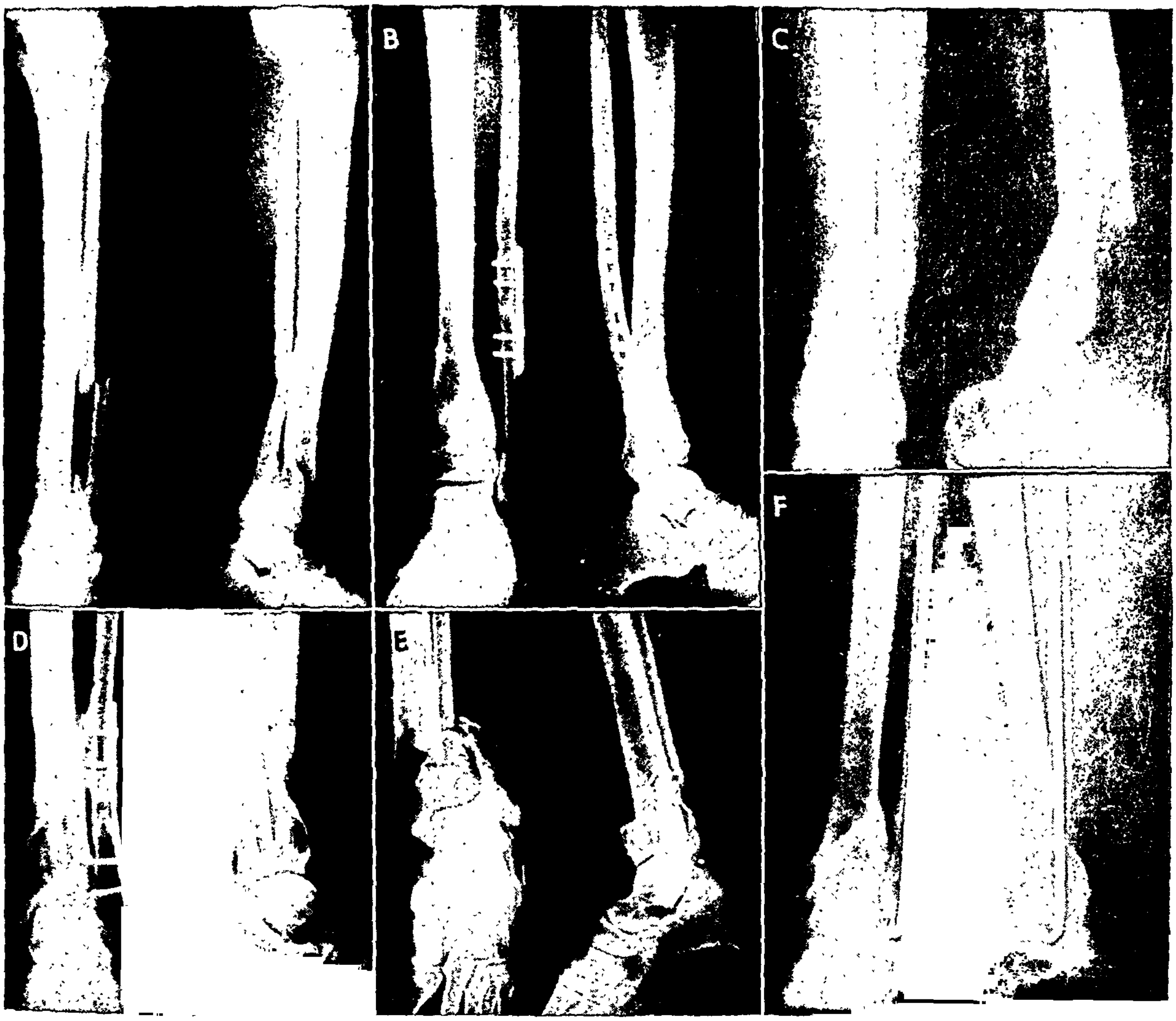

Fig. 2.—*A*, roentgenograms, dated Sept. 22, 1952, showing transverse compound supramalleolar fracture, with no joint involvement, in 45-year-old man. *B*, roentgenograms of patient in *A* showing appearance of fracture on April 14, 1958. Consolidation had occurred at four months. *C*, roentgenograms taken Jan. 7, 1955, showing a compound comminuted spiral-oblique supramalleolar fracture, with no joint involvement, in 43-year-old man. *D*, roentgenograms, dated March 25, 1958, show use of slotted plate to maintain reduction in fibula of patient in *C*. Consolidation occurred at six months. *E*, roentgenograms, dated July 15, 1957, showing compound supramalleolar fracture of compression type, with marked joint involvement, in 37-year-old woman. *F*, roentgenograms dated March 4, 1958, show reduction and control of short fibular fragment with Rush nail in patient in *E*. Consolidation occurred at four months.

carious. Because of the level of fracture, metal fixation of the tibia is usually impractical or ineffective.

Open reduction and fixation of the fibula for supramalleolar fractures has received reserved recognition in the literature. The most complete coverage of the subject is to be found in the French literature in the report of Rieunau and Gay,[6] in 1956, and in the monograph of André Mony [7] in the same year. These men have used intramedullary fixation exclusively with success, and their observations are very much the same as our own.

The fibular involvement in these fractures is often less than that of the tibia, there being a simple or a moderately comminuted closed fracture. If the fibula is reduced and stabilized, the fracture is then in a sense one of the tibia alone; tibial length is restored, fragments may be to some extent controlled or manipulated, and alignment is often surprisingly good. It should be remarked that restoration of length and alignment is important even in those cases for which ankle fusion is anticipated later. That most of these fractures are open makes even more desirable the fixation of the fibula, which may be approached through untraumatized tissue.

TABLE 2.—*Analysis of Supramalleolar Fractures*

Case No.	Classification		Joint Involvement	Fixation	Consolidation, Mo.	Results	
	Type	Condition				Anatomic	Functional
1	Transverse	Open	...	Plate	3	Poor	Excellent
2	Transverse	Open	2+	Plate	6	Fair	Good
3	Spiral-oblique	Open	...	Plate	6	Fair	Excellent
4R	Compression	Open	4+	Nail	4	Poor	Fair
4L	Compression	Closed	4+	Plate	Nonunion	Poor	Fair
5R	Compression	Closed	4+	Plate	4	Fair	Poor
5L	Compression	Closed	4+	Nail	4	Fair	Fair
6	Spiral-oblique	Open	2+	Plate	6	Fair	Good
7	Spiral-oblique	Open	...	Plate	4	Fair	Excellent
8	Compression	Open	2+	Nail	4	Fair	Good
9	Transverse	Closed	+	Plate	4	Fair	Excellent

If the fragments will accommodate a plate, this type of fixation is used; if the distal fragment is short, intramedullary fixation is used. Application of a plate is favored when this is possible because the procedure necessitates but one incision and because the extreme narrowness of the medullary cavity in some fibulas makes difficult the introduction of a pin or nail of adequate caliber. Shortening of the fibula may be necessary in fractures where there is loss of tibial substance or tendency to medial settling.

The stability gained with fibular fixation facilitates plaster application. After open reduction a long-leg posterior plaster splint or bivalved circular plaster is used. Straight long-leg circular plaster is applied after suture removal and subsidence of swelling. Some effort should be made to control with plaster any tendency of the fracture to settle.

Of the 11 fractures (table 2) in our series, 3 were of the transverse, 3 of the spiral-oblique, and 5 of the compression type. Three were treated with intramedullary nails and eight with slotted plates. The time of fracture consolidation has varied from three to six months from the date of operative reduction. There has been one nonunion in an individual with fractures of both legs. In this instance fibular fixation was also used in the secondary grafting procedure.

Anatomic results have often been poor; functional results have, on the whole, been gratifying (table 2). Patients with malalignment or marked joint involvement have been encouraged to use canes and have been made aware of the possible future need for joint stabilization. One secondary ankle fusion has been performed because of pain.

Diaphysial Fractures

In 1927, Charles Farr, in a short discussion of fractures of the tibia and fibula, stated that, "in selected cases of fracture of the tibia and fibula, notably when the tibia is badly comminuted or compounded and especially when infection has set in, it is possible to operate upon the fibula alone." Butterworth and Clary,[8] in 1945, reported the use of fibular fixation in 9 of 179 combat fractures of tibia and fibula because of loss of tibial length or substance due to marked comminution and compounding. The procedure was carried out initially as a temporary or emergency measure, but the results were so satisfactory that this method was adopted as definitive treatment for all such fractures. Carpenter and others,[9] in 1952, listed in their report 24 leg fractures treated by open reduction, with fibular fixation being the method of choice in 6 of these fractures. Coughlin,[10] in 1955, reported satisfactory results in three cases of comminuted compound fractures of tibia and fibula treated by means of fibular fixation.

Our own experience is limited to one compound fracture with severe comminution (fig. 3*A* and *B*). In this case a 5-in. slotted plate was applied to the fibula on the day of injury, the approach being through intact soft tissue. The compounding wound was cleaned, the tibial fragments were molded slightly, and the wound was closed. The wound healed primarily. Walking was permitted in plaster at 6 months, and consolidation was complete at 11 months. There is moderate posterior bowing, but the functional result is good. It is our opinion that the stability achieved in this case by means of fixation of the fibula aided in control of infection, promoted healing, and significantly reduced the morbidity.

Transcondylar Fractures

Transcondylar fractures or fractures of the proximal end of the tibia which are associated with overriding fractures of the fibula may be corrected with reduction and stabilization of the fibula. This possibility is illustrated in a case of this sort in which reduction of the fibula alone corrected rather accurately the tibial alignment (fig. 3*C* and *D*). A fault in operative technique rather than poor choice of method accounts for the loss of the original excellent position (fig. 3*E*). Loosening of the screws in the splint allowed migration of the fibular fragments and resulted in loss of reduction in the tibia. *This situation* illustrates well the need in certain cases to fix the fibula rigidly. The plaster in this instance did not control the settling. As a consequence the knee is in valgus and the functional result is fair.

The restoration of alignment in the original reduction in this case was possible because of the intactness of the proximal tibiofibular articulation which allowed the fibula to lift the proximal tibial fragment back into position.

Nonunion

Of our three cases of failure of union, infection occurred in two. In the third case, as previously

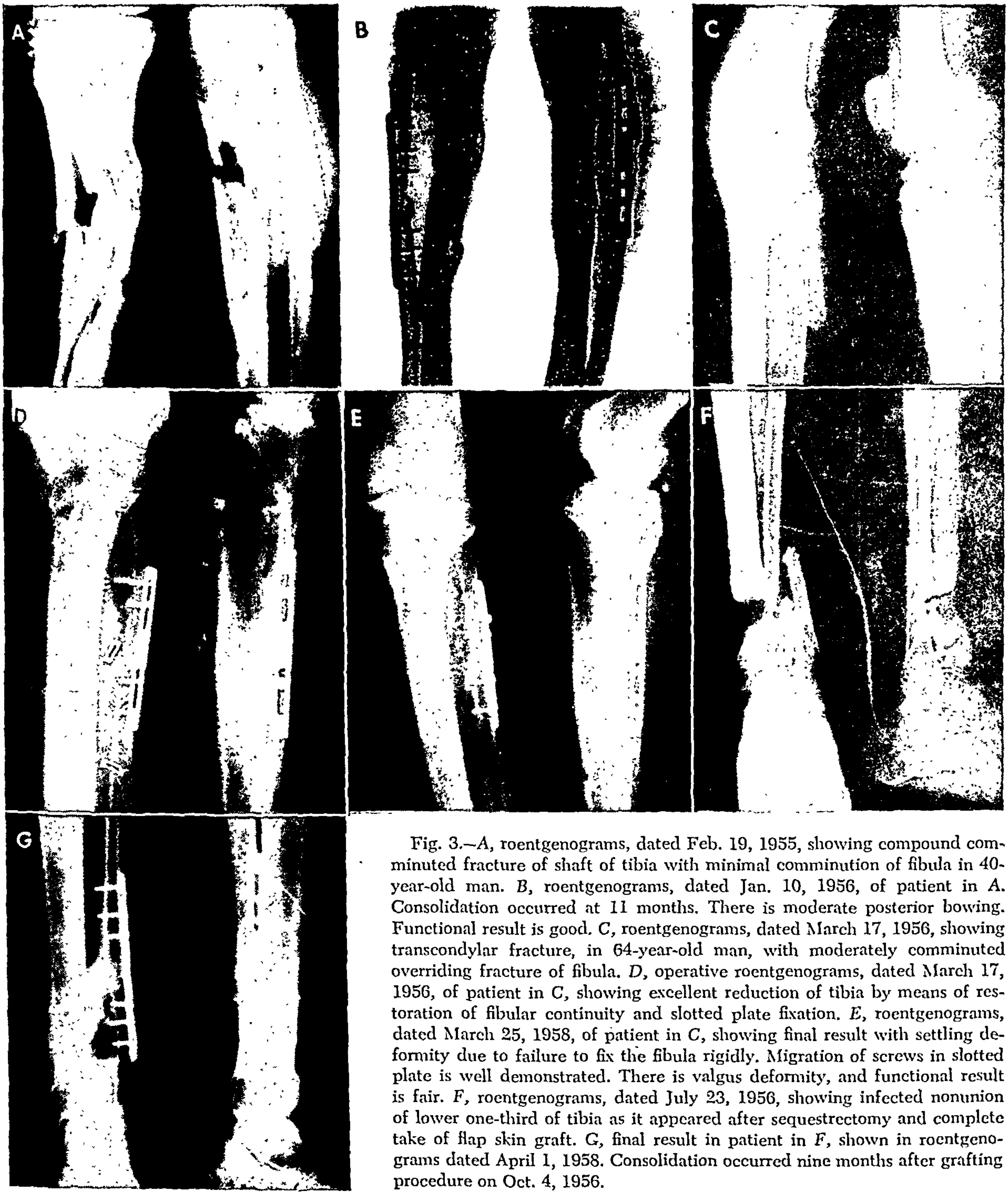

Fig. 3.—*A*, roentgenograms, dated Feb. 19, 1955, showing compound comminuted fracture of shaft of tibia with minimal comminution of fibula in 40-year-old man. *B*, roentgenograms, dated Jan. 10, 1956, of patient in *A*. Consolidation occurred at 11 months. There is moderate posterior bowing. Functional result is good. *C*, roentgenograms, dated March 17, 1956, showing transcondylar fracture, in 64-year-old man, with moderately comminuted overriding fracture of fibula. *D*, operative roentgenograms, dated March 17, 1956, of patient in C, showing excellent reduction of tibia by means of restoration of fibular continuity and slotted plate fixation. *E*, roentgenograms, dated March 25, 1958, of patient in *C*, showing final result with settling deformity due to failure to fix the fibula rigidly. Migration of screws in slotted plate is well demonstrated. There is valgus deformity, and functional result is fair. *F*, roentgenograms, dated July 23, 1956, showing infected nonunion of lower one-third of tibia as it appeared after sequestrectomy and complete take of flap skin graft. *G*, final result in patient in *F*, shown in roentgenograms dated April 1, 1958. Consolidation occurred nine months after grafting procedure on Oct. 4, 1956.

mentioned, treatment was also by means of fibular fixation as an acute fracture. One of the infected fractures is used for illustration.

The patient, who originally had an oblique compound fracture of the lower one-third of the tibia, was first observed one month after injury when there was ulceration over the fracture site with exposure of a metal plate. The plate was removed, the wound cleaned, and a plaster cast was again applied. Six months later a sequestrectomy was performed, and during the same admission a flap graft was applied to the skin defect. Fifteen months after removal of the original plate (fig. 3*F*), the site of nonunion was exposed and grafted with iliac bone, the grafts being placed liberally between the two bones. The fibula was shortened to allow approximation of the tibial fragments, and stabilization was obtained by means of a slotted plate applied to the fibula. Consolidation occurred nine months after operation. Figure 3*G* shows the final follow-up roentgenogram. The functional result is good.

It is noteworthy that, in some cases of infected nonunion, stabilization of the area by means of fibular fixation—the tibial site remaining undisturbed—enhances the possibility of healing and resolution of infection.

Surgical Approach

The fibula is easily accessible throughout its length in the plane between the peronei anteriorly and the triceps surae posteriorly. In the region immediately superior to the external malleolus, the peroneal tendons are retracted posteriorly. The incision at any level may follow an imaginary line extending from a point just behind the external malleolus to one just behind the head of the fibula. The common peroneal nerve must be isolated and protected in approaches to the upper end, and occasionally one encounters, at the distal end, branches of the musculocutaneous nerve.

Summary and Conclusions

Open reduction and fixation of the fibula in certain difficult fractures of both bones of the leg is an anatomically sound procedure. Our experience has shown that fixation of the fibula is an effective method of treatment in the following four distinct leg fracture problems: supramalleolar fractures, badly comminuted or compound diaphysial fractures, transcondylar fractures, and fractures with nonunion or malunion.

When indicated, open reduction and fixation of the fibula has the general advantages of (1) converting a fracture of both bones to one of the tibia alone, (2) restoring to the tibia length, alignment, and stability, (3) facilitating manipulation and eliminating undue handling of tibial fragments, (4) allowing approach through untraumatized skin and soft tissue in compound fractures, (5) affording stability for grafting in nonunions, (6) enhancing the efficiency of plaster and simplifying its application, and (7) reducing morbidity.

Addendum

Recently we have splinted the fibula in a comminuted segmental fracture of the tibia, soft tissue damage precluding tibial fixation. Length and alignment are well maintained.

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BALANCE AMONG THE SCIENCES.—It seems . . . much more probable that human happiness will come from discoveries in the biological sciences than from discoveries in the physical sciences. If there were a choice between a cure for cancer and economic nuclear power—most of mankind would choose the cure for cancer. As a corollary, it seems . . . inescapable that the current preponderance of mankind's scientific effort toward the physical, rather than the biological, sciences is wrong. . . . I would consider this to be one of the most important public responsibilities of science at large: to redress the balance between the physical and biological sciences, to direct more of the world's scientific resources along lines which are more nearly concerned with the issues of human happiness.—A. M. Weinberg, Prospects in International Science, *Bulletin of the Atomic Scientists,* December, 1958.

UPPER ARM BLOCK ANESTHESIA IN CHILDREN WITH FRACTURES

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Regional block anesthesia is especially useful for fractures of the arm in children. The technique here recommended involves an axillary route instead of the supraclavicular route. When the injection is made the proximal part of the humerus is used as a "backstop," and the terminal portion of the axillary artery serves as a constant and convenient landmark; the median and musculocutaneous nerves lie anterolateral to the artery, while the ulnar and radial nerves lie respectively anterior and posterolateral to it. Using this site for the injection eliminates the danger of pneumothorax, and by producing a sympathetic blockade it improves circulation in the arm. The present series of 80 patients with fractures included 72 children 10 years of age or under. Premedication consisted of pentobarbital given intramuscularly. The anesthetic used was lidocaine (Xylocaine) hydrochloride in 1.5% concentration with epinephrine 1:100,000, and the average volume injected was 10 cc. With the moderate sedation used and the reassurance of freedom from pain, the overwhelming majority of the patients have been extremely cooperative.

An effective, safe, simple method of brachial block anesthesia is desirable. The advantages of a conscious patient who can take care of his secretions and, if necessary, go home directly after simple fracture management are quite evident. The most important consideration is, of course, the full stomach. The majority of children we see with arm fractures qualify immediately for a block, because the child with an empty stomach is virtually nonexistent. There is probably no physician who does not know of some instance of death or serious complication occurring after the use of general anesthesia for a fracture in a patient who had a full stomach, vomited, and then aspirated. We further believe that the parent's best information on the time of last food ingestion is poor information, because of the inherent nature of children to eat incessantly. One additional fact that needs emphasis is that once the injury occurs all digestion stops for a period of many hours—at least six hours, and this is a minimum figure. Thus, even a six-hour wait after injury does not entirely lessen the hazard of general anesthesia. The use of narcotics in the immediate post-traumatic period also further prolongs the retention of gastric contents. Lavage of the stomach is an ineffective procedure because of particle size. Induction of vomiting, by either drug or direct pharyngeal stimulation, is unpleasant and gives no assurance that the stomach is empty.

Advantages of Block by Axillary Route

The use of brachial block by the usual supraclavicular route in patients of all ages has been a generally unsatisfactory procedure because of the far too frequent complication of pneumothorax. In addition, the hazard of subclavian artery hematoma is ever present. Both of these lead to further hospitalization, and this is most certainly contrary to the purpose of any block.

In 1949 Accardo and Adriani[1] presented a technique of blocking the brachial plexus by an axillary route. The method involves the use of the proximal humerus as a "backstop," instead of the first rib or the pleural dome, and utilizes the terminal portion of the axillary artery as a constant and easy to locate landmark rather than the indefinite measurements of the midpoint of the clavicle and "one fingerbreadth above" (fig. 1).

At the level of the insertions of the pectoralis major anteriorly and the latissimus dorsi posteriorly, the terminal portion of the axillary artery is palpable. At this level the nerves are still so centripetal that, with use of the artery as a landmark, the nerves are easy to block. The median and musculocutaneous nerves and their sensory cutaneous components are anterior and anterolateral to the artery; that is to say, they are "above" and "above and beyond" the artery. The ulnar nerve is inferior to, or "below," the artery. The radial nerve is posterolateral, or "below and behind," the artery.

With the arm at 95 degrees abduction from the body and in neutral rotation, the artery is palpated at the level of the insertion of the pectoralis major, and a skin wheal is raised directly over the artery, the physician making sure that the needle bevel is down and that the local solution is coming from the end of a 1-in. 25-gauge needle as it enters the skin. The needle is then directed above the artery, and 2 to 4 cc. of drug is deposited above, and above and beyond, the artery. The abduction is maintained, the needle is withdrawn to the subcutaneous area, and the arm is put into considerable external rotation at the shoulder. The needle is reintroduced below the artery, and 1 to 2 cc. of drug is deposited; then the needle is advanced virtually to the humerus so that it is below and behind the artery, and 2 to 4 cc. of drug is deposited. Aspiration is performed before each injection. Needle and

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humerus should be at a 90-degree angle. If a paresthesia is elicited, an injection of 0.5 to 1 cc. of drug is done promptly at this position; paresthesias are not deliberately sought. It has been our experience that the median and musculocutaneous nerves are much easier to block with the arm in neutral rotation; likewise, the ulnar and radial nerves are much easier to block with the arm in considerable external rotation (fig. 2).

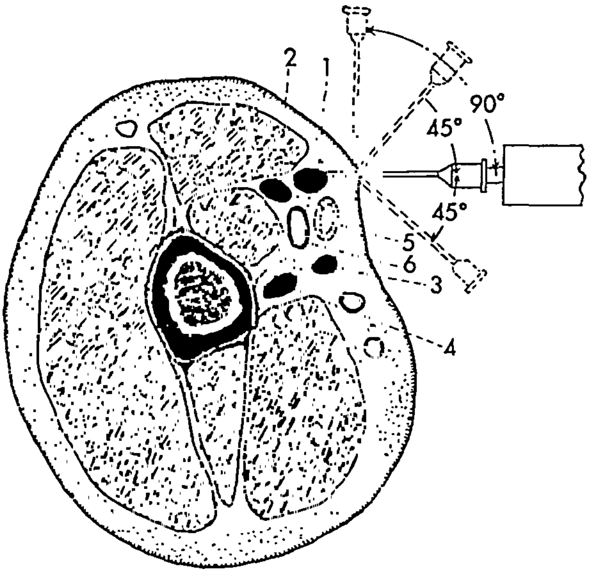

Fig. 1.—Brachial plexus block by axillary route. Cross-section is at junction of axilla and arm (through line 1, fig. 2). 1, median nerve; 2, musculocutaneous nerve; 3, ulnar nerve; 4, radial nerve; 5, brachial artery; and 6, vena comitans.

We have, in general, used injectable pentobarbital for premedication in these children. Those patients weighing less than 40 lb. (18 kg.) have been given 1 mg. of pentobarbital intramuscularly per pound of body weight; those weighing more than 40 lb. have received 0.6 mg. per pound, to a maximum of 50 mg. One-half is used for intravenous administration. This dosage will give moderate sedation in the average child, but he will be awake and cooperative. The objection has been voiced occasionally that children are not fit candidates for block procedures. We have not found this to be the case; in fact, with the moderate sedation outlined above and the reassurance of freedom from pain, the overwhelming majority of the patients have been extremely cooperative.

Another advantage of the block is the sympathetic blockade that develops to the periarterial sympathetic chain, as well as to the sympathetic fibers in the nerve trunks themselves. This results in an improved circulation, which is of benefit in such vascular-compromising fractures as the severe supracondylar fracture. A secondary benefit is the more rapid resolution of soft tissue edema adjacent to the fracture site. The site of injection, of course, makes a pneumothorax impossible, and the use of a 25-gauge needle virtually eliminates the chance of a hematoma.

Summary of Cases

In a total of 80 patients indication for the block was fracture of distal one-half of the humerus in 17, fracture of the radius and/or ulna in 41, fracture of the hand or fingers in 6, tendon transplants in 3, soft tissue surgery below the midhumerus 12, and diagnostic 1. Of these 80 patients, 72 were 10 years of age or under. The youngest patient was 6 weeks of age and had markedly displaced fractures of the radius and ulna. In the 80 cases there was only one in which the block was not effective; this was an open reduction of a supracondylar fracture. The reason for this failure is not clear, because the patient was checked with needle point before the incision was made. The only explanation we have is that this might have been innervated by some aberrant branch from the cervical plexus. Occasional difficulty has been encountered in blocking the musculocutaneous nerve; it was found at operation that external rotation of the shoulder has a positive tendency to swing the nerve considerably laterally from the median nerve, which remained close to the artery.

We have used 1.5% concentration of lidocaine (Xylocaine) hydrochloride with epinephrine hydrochloride, 1:100,000, in most of these cases. We thought it preferable to use the 1.5% concentration because of the more profound anesthesia it could afford the patient and because of the possibility that it might further potentiate the tissue penetrating quality that lidocaine is felt to have. We chose to use it with epinephrine because of the much slower absorption, which might protect the patient from a drug reaction.

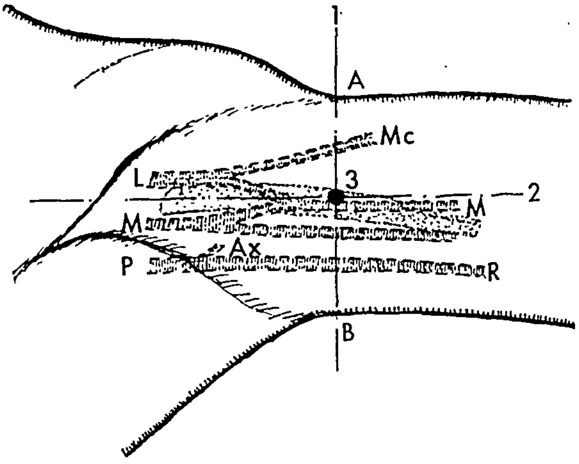

Fig. 2.—View of axilla showing landmarks for brachial plexus block by axillary route. Line 1 is drawn through points of insertion, *A*, of pectoralis major and, *B*, of teres major muscles into the humerus. Line 2 bisects line *AB* and falls directly over brachial artery. Wheal is raised at point 3. *L* is lateral cord of plexus, *M* medial, and *P* posterior; *Mc* is musculocutaneous nerve and *R* radial nerve. Note that axillary nerve *Ax* has been given off before site of block.

In this series of 80 cases, we had only one minimal reaction, that of twitching at the corners of the patient's mouth; she had received 20 cc. of

2% solution of lidocaine, which is more than we would now use. The reaction was easily treated with a small amount of pentobarbital given intravenously; oxygen is also always kept available for use with any possible reaction. Our average volume of drug used was 10 cc. The smallest volume used was 1.5 cc. in the 6-week-old baby. If one wishes to use a tourniquet, a narrow subcutaneous "bracelet" of a weaker solution of drug is placed around the arm at the level of the block. Anesthesia of the fibers from the cervical and thoracic roots that are not parts of the brachial plexus will result.

If one and one-half to four hours of anesthesia are desired, 1% solution of tetracaine (Pontocaine) hydrochloride is added to the lidocaine, so that the final mixture has 1.5 mg. of tetracaine per cubic centimeter of solution. This will give a quick onset from the lidocaine and duration from the epinephrine and tetracaine. The tetracaine is available in 20-mg. (2.0-cc.) ampuls.

Conclusions

Brachial block anesthesia by the axillary route, as described by Accardo and Adriani,[1] is an excellent, safe method of regional anesthesia. The nerve supply of the arm is blocked without the possibility of thoracic complications. Thoracic complications from supraclavicular blocks are quite frequent and at times serious.

This block has been especially useful in the treatment of recent fractures in children, as one may assume there is food in the child's stomach and therefore a risk of aspiration if general anesthesia is used. The resulting sympathetic block is also of value in certain cases, e. g., supracondylar fractures of the humerus.

The technique is simple. Children have not objected to the technical use of the needle and have cooperated well. In 80 consecutive cases there has been only one failure. It is interesting to note that, of these cases, twenty-seven occurred during the months of April and May, 1958. This indicates the growing interest in this type of block anesthesia in our locality, although we have been using the method since 1954.

899 Detroit St. (6) (Dr. Turner).

Figures 1 and 2 are reproduced, with permission, from "Nerve Blocks," by John Adriani, Springfield, Ill., Charles C Thomas, Publisher, 1944.

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THE RESIDENT AND THE MEDICAL STUDENT

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The resident is generally presumed to play some part in the hospital educational scheme, especially since emphasis on bedside teaching is increasing. His role in the educational team may not be evident to him, to his senior colleagues, or to the medical student. His abilities and obligations need to be more adequately defined. This will enable him to make an orderly approach to basic principles, to develop teaching skill, and to exercise initiative. He can use ancillary teaching methods, such as reading assignments or conferences, that can be very effective as supplements to ward rounds. Efficient communication of significant information thus becomes a greater reality to the educational team, with improved care of the sick as the ultimate goal.

As students progress through the maze of medical training, they face new problems and increasing responsibility. They begin to appreciate more fully the concern teachers and senior colleagues show about their development. Furthermore, when the residency program is embarked on, a position is entered which requires the showing of concern for the junior colleagues, the medical students. Residents in teaching hospitals have as regular responsibilities not only patient care but also teaching interns and medical students. Teaching responsibility is stimulating but also somewhat ambiguous. In an attempt to clarify what teaching responsibility at the resident level means, I shall draw on my own brief experiences and on the experiences of my colleagues on the resident staff of Presbyterian-St. Luke's Hospital in teaching medical students within the framework of the case method. I hope this will encourage other residents

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and also visiting physicians to make their thoughts on the subject available to residents, interns, and medical students.

As residents, we learn to teach because we must and, to varying degrees, because we enjoy it. That our senior colleagues are interested in our learning to care for patients is evident. However, they are also interested in our becoming good teachers; the resident was made an integral part in undergraduate teaching programs when the emphasis in teaching third and fourth year medical students was shifted from formal lectures to medical clerkships. Originally, the residency program existed for the sole purpose that residents might learn patient care. Now the program has expanded to the extent that residents must also be teachers.

The following questions seem particularly pertinent to the resident-medical student relationship: What part is the resident to play on the educational team? How should he carry out this part? Can residents as a group develop and maintain a scholarly tradition in medical student teaching by complementing the efforts of the senior faculty members involved in clerkship teaching?

The Resident's Role

As I began my medical residency, I understood little of what would be expected of me as a teacher; however, as my residency has progressed I have come to a fuller realization of the challenge evoked by teaching medical students—one which certainly taxes a resident's resourcefulness. On the basis of brief experience, I would suggest that the answer to the previously stated questions may be found by reflection on the resident's exact role in relation to the "professor" (or chief of service) and the medical students.

To borrow from cybernetic terms, the resident's function at a glance seems best described as that of a bridge of communication between the medical student and the "professor"—or that of a two-way transmitter. The basic difficulty in this function concerns the kind and extent of modulations of messages transmitted either way. In particular, how far should a resident go as a sorter of information, and how free in this function should he be to draw generally on medical information and teaching methods? The answers to these questions are of necessity related to the basic foundations of any educational process, teacher-student bonds, and, also, local hospital arrangements and individual personalities.

The answers do not come easily. For example, what Wiener[1] would call "jamming" in cybernetics seems to appear in two recent papers on medical education. The first paper, "Adventure in Pedagogy,"[2] submits the hypotheses that "teachers may be major obstacles to student learning," that "people learn what they want to learn," and that "true learning is largely an emotional experience." It also states that a majority of the people involved in the seminar on which this article is based were provided "with a satisfaction they had not previously known." The nature of the "satisfaction" is not clear.

The second paper, "Disaster in Pedagogy,"[3] is a rebuttal to the first. The author agrees that medical education should be improved. However, he submits that the stimulus for improvement comes from higher to lower levels through the maintenance of scholarly standards and not through an abused concept of "educationist's freedom."

The resident's position does not allow him to decide the final answers to these arguments. However, as residents we should have some definite approach toward our job of teaching medical students. Therefore, it seems to me that we might look to some reasonable authoritative basis in deciding on this approach. So far as the hypothesis that "learning is largely an emotional experience" is concerned, I would agree from personal experience that at certain times emotional factors influence efficiency in learning. But I do not agree that learning is "largely" emotional. Even in the area of religion, where some degree of emotional experience is evident, the importance of rational thought, logical argument, and scholarly standards is emphasized.[4] In medical education the maintenance of scholarly standards presupposes adequate leadership and also an effective system of communication between the leader (professor or chief of service), the resident, and the medical student.

Personally, I feel strongly that residents should draw on the experience of their senior colleagues, for experience implies that these individuals have made mistakes from which they have profited immensely throughout the years. Therefore, they should be in a position to help avert similar mistakes by their junior colleagues.

Perhaps medical education in America today faces the challenge of "The Revolution in Education"[5] that has been described for other branches of education. In medical education, intellectual originality must not be stifled by inadequate communication; however, it is just as vital that one who communicates, especially if it is his life's career, should have something to say based on a degree of intellectual originality.

My reasons for setting down my thoughts on medical education with special reference to the resident–medical student relationship are several. First, the literature on medical education with which the average house officer and medical student have intimate contact contains a paucity of clearly defined principles regarding this vitally important subject.

Second, in medical schools where clerkship teaching is a major part of the curriculum, it is mandatory that the resident be interested and capable to some degree as a teacher.

Third, although I feel that more enlightened residents are cognizant of this, the resident–medical student relationship properly effected is of practical advantage. That is, aside from the transmission of information from the resident to the medical student, the medical student's presence and questions are a constant stimulus against the resident's succumbing to intellectual lethargy—just as the latter's continuous questioning of the professor is at another level. Likewise, the student profits in this system by more clearly finding his "self-image,"[6] in that he becomes an integral part of the patient-care and educational teams.

Fourth, it is important that the resident form an individual philosophy or school of thought regarding his position in relationship to the professor, intern, and medical student. The hippocratic oath clearly charges every teacher to aid his junior colleagues, but the present structure of the clerkship program requires some further crystallization of the relationship of each member of the educational team. Often, the resident seems to be a "middleman" or a two-way transmitter of messages, at least as far as daily contact with medical students is concerned. This function seems valid, but only if it is accompanied by direct contact between the professor and the medical student and also if it allows the resident to express whatever awareness, resilience, and fertility of mind he may possess. In short, the resident should not be the professor's "yes man."

Fifth, the physician is, in one sense, a biological scientist. And, as Richardson[4b] has aptly stated, he "needs to know much about biochemistry, and therefore about chemistry, and therefore about physics, and therefore about mathematics. . . . The comparative study of the sciences . . . helps us to see why the methods that are highly efficacious in one science are not useful in another." Therefore, to focus attention on a discipline which itself is concerned with a high degree of integration might be useful, and consequently the ensuing discussion is in terms of communication.

Problem of Communication

There are several apparent areas to which these concepts of communication can be applied. First, there is the matter of curriculum revision manifest in recent years by the increasing amount of bedside teaching at the medical student level with an accompanying decrease in formal lectures. The resident has not been involved in making this decision, but he has been directly affected by it. With this transition the resident has been thrust into a position of greater responsibility in teaching medical students; however, he may not have been impressed with this change, and his senior colleagues may not have evaluated his abilities and obligations adequately. Thus, in cybernetic terms there is a break in the bridge of communication, and this allows entropy to increase.[7] There is much in favor of clerkship teaching, but only when adequate emphasis is given to the necessity of reading and discussion and the degree to which the resident, intern, and medical student must participate.

Second, the resident might do something in addition to discussing patient problems on ward rounds with the medical students if he is to realize fully his potential in "communicating" with the medical students. The resident in the junior year can often benefit from the advice and experience of senior colleagues in effecting ancillary teaching methods. Often the matter may rest entirely with individual initiative and abilities of each resident, which may or may not be conducive to an orderly approach to understanding the application of basic principles.

Third, the importance of the integrity of the educational team may not be evident either to the resident or to the medical student. As is true with the "burn" team, the "cardiac catheterization" team, the "research" team, and the "patient-care" team, the members of the educational team should clearly understand the problems they face and the individual responsibilities they have in meeting these problems. Only by precise delineation of responsibility for each member of the educational team can effective communication be achieved and the tendency toward increasing entropy be abated. I wish to suggest that perhaps a portion of the solution of the questions concerning teacher-student contact may be achieved by more exact examination of cybernetics and the concept of entropy versus order. McCulloch[8] has recently alluded to the discrepancy between the number of afferent and efferent messages passing through the cerebral cortex (the former being by far the greater), and from his discussion we may infer the influence of coincidence as well as the influence of the number of useless messages on this discrepancy. We may now consider the practical importance of cybernetics in medical education.

Cybernetics in Medical Education

"Just as entropy is a measure of disorganization, the information carried by a set of messages is a measure of organization. . . . The information carried by a message [is] essentially the negative logarithm of its probability."[1]

An example of the quotation from Wiener's "The Human Use of Human Beings" is "Cancer is a bad disease." This statement has a high degree of probability in a number of situations; however, the statement "Nucleosides decrease erythrocyte osmotic fragility in hypotonic phosphate" is true for a much smaller number of situations and yet conveys more information. Effective education is concerned with the transmission of messages with significant information. Therefore, the maintenance of scholarly standards requires efficient communication. Two possible impediments to communication and effective education are the increasing size of medical school classes and the lack of interest in medical students on the part of an occasional resident. These impediments enhance the tendency toward increasing entropy.

Schrödinger,[7a] Wisdom,[9] McCulloch,[8] and Mascall[4a] have recently dealt with the more basic arguments on the definition and implications of the term entropy. Schrödinger, referring to Gibbs and Boltzmann, has expressed the statistical and sociological connotations of entropy by the formula, "entropy = k log D," where k is a constant and D a measure of disorder. Thus order is the reciprocal of entropy.

Due to the vastly increasing macrocosm of messages (facts or observations) to which we in medicine are continuously exposed, we are forced to reflect seriously on what material or messages are significant and essential and, consequently, how our methods of clerkship teaching can best resist the tendency toward increasing entropy. I wish to state candidly that I am not proposing that all medical educators devote their entire efforts to teaching methods, for such a proposition effected might result in the "progressive" undermining of the educational process which some observers[3] feel has occurred in our lower schools through the efforts of the "educationists." What I am proposing is an increasing awareness on the part of the resident's senior colleague, the professor or chief of service, of the relative positions of the resident, intern, and medical student on the educational team; this consideration will permit a certain degree of autonomy on the part of the resident in teaching and learning (i. e., as a transmitter and sorter of messages who can draw on contingent sources for information as well as directly from his senior and junior colleagues).

The resident has the obligation and responsibility of helping his senior colleague, the professor, in "getting the message across" to the medical student that he is an integral part of the patient-care and educational teams. As Keefer states,[10] "One of the important functions of the house staff is to join all other members of the group in the educational process of the undergraduate medical student." Caseley[10A] has also emphasized that the resident's "teacher-role" has often been taken for granted, and he has implied the necessity of more careful assessment and encouragement of the resident in this capacity. Osler,[11] in his address "Teacher and Student," has amply and succinctly defined the qualities prerequisite in a teacher, namely, "enthusiasm," "knowledge of the branch taught," and a "sense of obligation." He also considered personal contact between teacher and student to be essential. The resident may not have advanced to the state of knowledge of his seniors in a given subject, but he is totally capable of enthusiasm and a "sense of obligation."

Experience in Medical Clerkship Teaching

During our residency (and throughout our entire careers), we must grow in assuming responsibility for patient care and also in assuming teaching responsibility.[12] We gradually develop skill in teaching and learning (transmitting and sorting information), just as we develop skill in diagnosis and therapy. Both skills seem almost inextricably bound. How, then, can we best help to "get the message across"? At this point I wish to cite some of the experiences which have been noted in medical clerkship teaching at Presbyterian-St. Luke's Hospital with the University of Illinois senior medical students, particularly at the resident-medical student level.

First, attempting to cram a multitude of unrelated facts (or messages) into one's head is futile without some concept of basic principles (how to sort and classify messages or information). The professor (or chief of service or attending staff member) largely has the responsibility of emphasizing and clarifying these basic concepts by direct contact with the medical student. The resident is responsible for reiterating these concepts in light of their application to individual daily patient problems. From this it follows that the resident and medical student alike will investigate further these concepts by reading critically the fundamental literature on a given subject, which incidentally, is not necessarily synonymous with the latest journal article published. Subsequent investigation, discussion, and argument then provide the members of the educational team with greater intellectual enlightenment (i. e., by critically sorting and reclassifying significant messages and information) and will result in better patient care.

There are several ancillary teaching methods which, properly implemented, can be very effective. These are not new methods, but they have been used as supplements to ward rounds in communication between residents and medical students (i.e., in transmitting, sorting, and classifying information). Among these are student journal club, "coffee-break" 10-minute talks by medical students, outside subject study assignments, and "quizzes." These maneuvers have been tried by the resident staff for a period of time and have been pleasantly successful.

Student journal club, to which one hour each week has been devoted, consists of two students discussing recent articles of general interest agreed on by the resident and the students. The 10-minute talk, originated by another of the residents, consists of a short dissertation on one subject related to a patient problem currently on the ward. Special subject home study assignments outlined by the residents consist of hypothetical case problems related to similar situations seen by the students or derived from cases with which the residents had previous experience. The quizzes, given twice each quarter, consist of short-answer written questions derived from standard textbook sources plus an oral examination given by the residents. The oral examination consists of questions in internal medicine, x-ray film interpretation, and general pathology with clinical correlation. Residents from the radiology and pathology departments participate in these quizzes. No "grade" is turned in, although the quizzes are gone over thoroughly with the students in order to point to areas of strength as well as weakness. These did not involve "spoonfeeding," for they pointed to areas of endeavor dependent on individual initiative and interest.

If these methods have been used successfully on previous occasions, the question arises as to why they should be more effective when utilized by residents than when utilized by senior faculty members. Perhaps they are not more effective when utilized by residents. There are some reasonable hypotheses regarding this question. One is that the resident may be more acutely aware of student deficiencies in the clerkship framework because of his more active student contact (i. e., the resident may have a given student on his floor or ward for three weeks with continuous daily contact or rounds). Another is that a given student may at times feel more free to raise certain questions with a resident than with a senior faculty member (this is not always true and does not imply that senior members of the educational team provide obstacles to learning). Third, the resident becomes intimately responsible for a portion of the medical student's intellectual development and benefits through this relationship by enhancing his own knowledge (by reciprocal transmission of messages with the medical student). Fourth, the individual medical student is evaluated at relatively infrequent intervals by the senior members of the educational team (i. e., in terms of examinations and final evaluation); the resident may be able to assist the student with certain difficulties in learning (sorting messages) at a point crucial to his final evaluation. These ancillary methods employed by the residents seem valid because they exist for the purpose of enabling the members of the educational team to become more proficient at interpreting data (sorting messages) and at classifying information and also for the purpose of ultimately improving patient care.

Conclusions

The resident's role on the educational team is important. His function is not only to transmit messages or information between the professor and the medical student but also to sort and modulate messages transmitted, to draw freely on general medical information, and to instill this information into the bridge of communication existing between the members of the educational team. Allowing the resident to exercise awareness, resilience, and fertility of intellect insures additional feeding of significant information into the pool of messages (or thought) transmitted along the bridge of communication and should help to insure maintenance of scholarly standards. Efficient communication of significant information then becomes a greater reality to the educational team. As Hutchins puts it, "A world community can exist only with world communications, which means something more than extensive short-wave facilities scattered about the globe. It means common traditions, common ideas, and common ideals." [13] I wish to submit that, through some consideration of the integrity of the educational team and the importance of efficient transmission of significant information in opposing entropy, our ultimate goal, optimal care of the sick, may be more nearly achieved.

I have alluded to some of our own "adventures in pedagogy," with emphasis on the transmission and sorting of significant messages or information by persons who have something to communicate and who are not merely concerned with the methods of communication. The resident is not the most experienced transmitter and sorter of messages on the educational team, but he does have an obligation as a teacher to do what is reasonably possible to aid the medical students for whom he is responsible. Thereby he broadens his own intellectual horizons, forms a sounder philosophy of human relations, and exercises a bit of Promethean will. Finally, the professor, the resident and intern, and the medical student should hold a consultation:

> A consultation comes in order next—
> You know what this is? In a certain place
> meet certain doctors to discuss a case
> and other matters, such as weather, crops,
> potatoes, pumpkins, lager beer, and hops.
>
> Rip Van Winkle, M.D.
> Oliver Wendell Holmes

1753 W. Congress St. (12).

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OPACIFYING GALLSTONES

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Certain biliary calculi become radiographically opaque after prolonged exposure to cholecystographic contrast mediums. The condition of prolonged exposure is fulfilled by the four-day iopanoic acid test. Opacification may be quite faint and recognized only by close scrutiny of the x-ray films. The four-day iopanoic acid test is a useful method for identifying bile duct stones. The test is, probably, the best available method for demonstrating bile duct stones in the presence of jaundice. The method is also helpful in identifying gallbladder stones in problem cases.

Certain gallstones become roentgenographically opaque after prolonged exposure to cholecystographic contrast mediums, with or without visualization of the gallbladder or bile ducts. We have called these calculi "opacifying gallstones."

Theander[1] observed the opacification reaction in an unproved case of cholelithiasis. We have reported proved cases of opacifying gallstones,[2] with in vitro reproduction of the phenomenon.[3]

X-ray Technique and Findings

Our observation of opacification of biliary calculi was made while exploring possible advantages of prolonged administration of iopanoic acid (Telepaque) in patients whose gallbladders could not be visualized or could be visualized faintly after the conventional examination with 3 Gm. of iopanoic acid. These patients were placed on a four-day regimen of 3 Gm. of iopanoic acid per day, 1 Gm. after each meal. A relatively fat-free diet was given during this period. The x-ray examination was made on the morning of the fifth day, with the patient fasting. We have called this prolonged preparation for cholecystography the "four-day Telepaque test." The test is well tolerated; diarrhea is controlled with paregoric. In one instance, opacification of biliary stones occurred with a similar regimen with iophenoxic acid (Teridax) used instead of iopanoic acid. We are exploring other variations of the four-day iopanoic acid test.

The opacified biliary calculi are usually characterized roentgenographically by a generalized faint increase in the over-all density of the stones and a sharp linear density outlining the periphery of the stones. The opacification of the stones may be quite faint and recognized only by close scrutiny of the x-ray films. When the iopanoic acid deposit on the surfaces of the stones is heavy, the density outlining the periphery of the calculus becomes thicker (fig. 1) and, occasionally, the stones appear homogeneously opaque (fig. 2). Most commonly, the opacification becomes evident on the third or fourth day of the iopanoic acid regimen, but, occasionally, it occurs on the second day and increases in intensity on the third and fourth days. In most instances of gallbladder calculus opacification, the gallbladder has been faintly visualized. When calculi in the bile ducts have been opacified, the ducts are usually not visualized. The opacification of calculi in the absence of visualization of the biliary structures indicates the marked sensitivity of this reaction. Usually, all stones in a patient with cholelithiasis are either opacifying or nonopacifying; less commonly, stones in the ducts are opacifying while stones in the gallbladder are nonopacifying in the same patient. We have not encountered an instance in which the stones in the gallbladder were opacifying and the duct stones nonopacifying. Rarely, one or more of the stones in the gallbladder or in the ducts are opacifying and the others are nonopacifying. After completion of the four-day iopanoic acid test, the opacification of the stones persists for a variable period of time, ranging from 2 to 14 days, and then they gradually fade to complete disappearance.

Clinical Evaluation.—We have examined 123 patients with this test whose gallbladders either could not be visualized or could be visualized faintly after the conventional one-day 3-Gm. iopanoic acid test. A review of the findings revealed that 76 had probable or proved calculous biliary tract disease, while 32 had noncalculous biliary tract disease and 15 had a normal biliary tract. There were 13 pathologically proved cases of bile duct stones in the 76 patients with calculous biliary tract disease. Ten of the 13 patients, or over 75%, showed opacifying stones in the bile ducts with (4 patients) or without (6 patients) opacifying stones in the gallbladder. Three of the 13 patients with proved bile duct stones showed no opacification either because of extreme jaundice or because the stones were of the nonopacifying type. Cholangiograms with intravenously given iodipamide (Cholografin) sodium were obtained at the time of the four-day iopanoic acid test in 3 of the 10 patients with opacifying bile duct stones. The ducts could not be visualized in two of these three. In six pa-

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tients, the opacifying stones were located in the gallbladder only. Nine of the 10 patients with opacifying bile duct stones had slight (bilirubin level, 1-2.5 mg. %) or moderate (bilirubin level, 2.5-5.0 mg. %) jaundice at the time of the four-day iopanoic acid test.

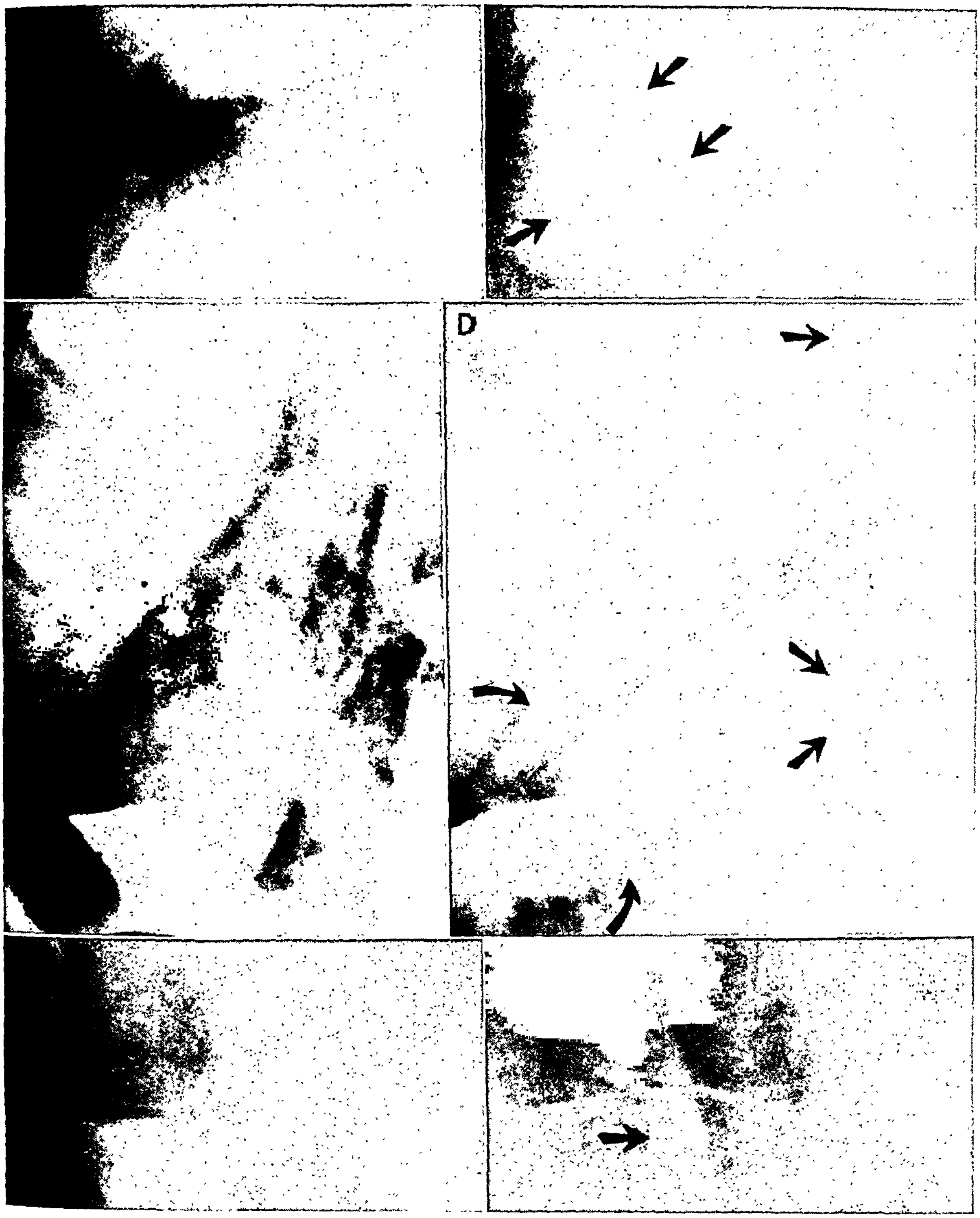

Fig. 1.—Roentgenographic results of test with 3 Gm. of iopanoic acid (Telepaque): *A*, after one day, no visualization of biliary structures and, *B*, after four days, opacification of three large gallbladder stones and faint visualization of gallbladder; *C*, after one day, no visualization of biliary structures and, *D*, after four days, opacification of three bile duct stones and faint visualization of ballbladder; *E*, after one day, no visualization of biliary structures and, *F*, after four days, opacification of solitary stone in gallbladder.

We have concluded from this analysis that the four-day iopanoic acid test is a useful method for identifying bile duct stones. The test is, probably, the best available method of demonstrating bile duct stones in the presence of jaundice, where cholangiography with use of iodipamide usually fails in visualization of the bile ducts.[4] In an occasional problem case, the test is helpful in identifying stones in the gallbladder.

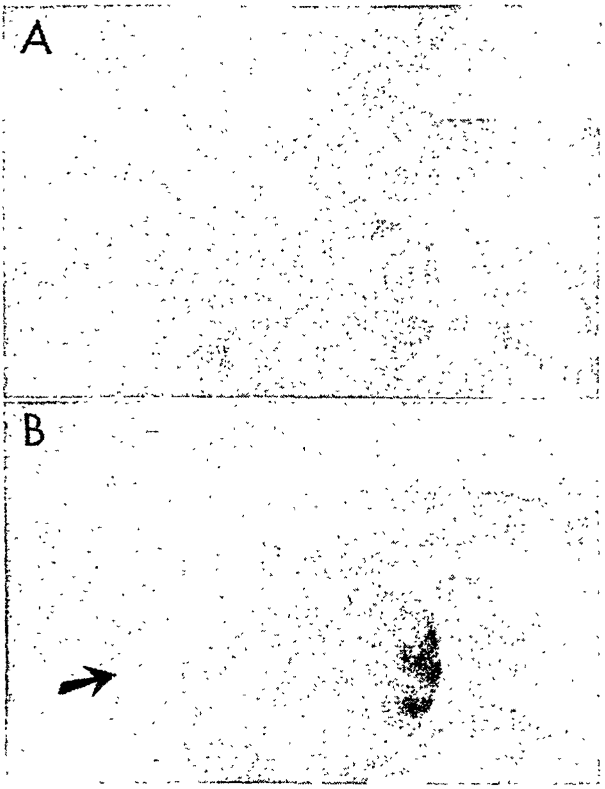

Fig. 2.—Roentgenographic results of test with 3 Gm. of iopanoic acid (Telepaque): *A*, after one day, no visualization of biliary structures and, *B*, after four days, opacification of solitary stone in bile duct, with no visualization of biliary structures.

In Vitro Studies

The phenomenon of gallstone opacification has been reproduced in vitro. Bile duct calculi, showing the opacifying quality clinically, have been obtained at autopsy in the unopacified state and subjected to further in vitro study. Samples of such bile duct calculi in the unopacified state and samples of clinically nonopacifying gallbladder calculi were immersed in plastic tubes containing bile with iopanoic acid and normal bile. The first sample was obtained at laparotomy from the gallbladder of a patient who had received 3 Gm. of iopanoic acid the evening prior to the operation. The normal bile was obtained at autopsy from a gallbladder of a normal person. The tubes were x-rayed immediately, kept at room temperature, and x-rayed four days later (fig. 3). The stones showing the clinical opacifying quality were strikingly opacified in the tube of bile with iopanoic acid. The clinically nonopacifying stones were not opacified in this tube. There was no additional opacification of the opacifying stones or of the nonopacifying stones in the normal bile. These experiments have led us to believe that the opacification of calculi is the result of a deposition of iopanoic acid on the surfaces of the stones and that the opacifying quality is inherent in the stone and not due to an instability of the colloidal system of the bile.

Further experiments have indicated that the clinical x-ray phenomenon of opacification of certain radiolucent biliary calculi with prolonged administration of iopanoic acid can be reproduced in vitro with opacifying calculi and buffered 2% solutions of iopanic acid, iodophthalein (Iodeikon) sodium, and phentetiothalein (Iso-Iodeikon) sodium simulating the concentration of gallbladder contrast medium in a visualized gallbladder. The reaction may also be reproduced with buffered solutions of iodoalphionic acid (Priodax), iophenoxic acid, and iopanoic acid, but with some difficulty because of the insolubility of these contrast agents. Most in vitro studies have been accomplished with these contrast mediums because of the difficulty encountered in obtaining iopanoic acid–opacified bile at operation. The opacifying reaction did not occur with clinically opacifying stones and buffered 2% solutions of potassium iodide, iodipamide, methylglucamine diatrizoate (Renografin), diprotrizoate (Miokon) sodium, acetrizoate (Urokon) sodium, sodium iodomethamate (Neo-Iopax), iodopyracet (Diodrast), and methiodal (Skiodan) sodium.

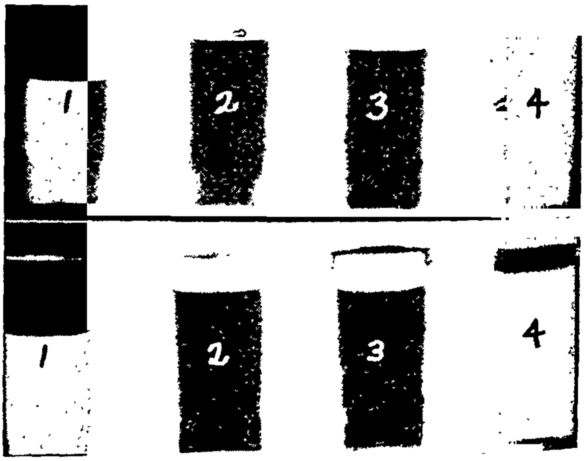

Fig. 3.—Results of test with normal bile and bile with iopanoic acid (Telepaque): (*top*) immediate x-ray, showing (*1*) gallbladder stones in bile with iopanoic acid, (*2*) bile duct stones in bile with iopanoic acid, (*3*) gallbladder stones in normal bile, and (*4*) bile duct stones in normal bile, and (*bottom*) x-ray after three days at room temperature, showing increased opacification only of bile duct stones in bile with iopanioc acid (*2*).

One hundred samples of biliary calculi found at surgery or autopsy at Denver General Hospital have been subjected to the in vitro test to determine the incidence of opacifying stones in this unselected group. Samples of each case of stones were immersed in a buffered 2% solution of iodophthalein sodium in plastic tubes. These tubes were x-rayed immediately, kept at room temperature, and x-rayed four days later (fig. 4). About 20% of stones collected in this manner proved to be opacifying. Grossly, the opacifying stones were always heavily pigmented, although not all pigmented stones proved to be opacifying.

Gallstone Type and Opacification Reaction

Aschoff[5] has classified gallstones into "pure" cholesterol, "pure" pigment, combined, infectious, and stasis types. The pure cholesterol stones are usually solitary and round and on section show a radiant structure of coarse cholesterol crystals. The pure pigment stones are multiple, black, small, and mulberry-shaped with amorphous structure. The combined stones are composed of a central pure cholesterol core with lamellar, peripheral layers of pigment, cholesterol, and, frequently, calcium. The infectious stones are generally multiple and faceted or lobulated. On section, these stones are lamellar and, frequently, fissured. The cholesterol-surfaced stones are yellow; the pigment-surfaced stones are dark brown to black. The stasis stones, usually found in the bile ducts, are frequently multiple, pigmented, and friable, consisting of a central infectious cholesterol stone core, which probably migrated from the gallbladder into the bile passages, and soft peripheral layers of pigment. Aschoff[5] described stasis stones as "earthy"; mud or gravel are common terms used to describe these calculi. Aschoff believed that the pigmented layers deposited on the surfaces of the cholesterol core result from the stasis of bile which accompanies bile duct stones.

The 100 cases of stones subjected to the in vitro test for opacifying quality were classified, as far as practical, according to Aschoff's terms, and the opacifying reaction of each classification was noted. All pure cholesterol stones were nonopacifying. All pure pigment stones were opacifying. Among the combined stones, there were nonopacifying and opacifying types. Among the infectious stones, all the yellow, cholesterol-surfaced stones were nonopacifying. The pigment-surfaced, infectious stones were both nonopacifying and opacifying. All stasis stones were opacifying.

Gallstones are essentially composed of varying quantities of cholesterol, inorganic salts (chiefly calcium carbonate and phosphate), and bile pigments (chiefly bilirubin and biliverdin).[6] A gallstone may be fractionated into these substances by their differential solubility in various solvents: cholesterol, ether; inorganic salts, hydrochloric acid; bilirubin, chloroform; and biliverdin, methyl alcohol. To determine which of the substances in an opacifying gallstone is responsible for the opacification reaction, an opacifying gallstone was fractionated into cholesterol, inorganic salts, and bile pigments. Samples of each fraction were immersed in plastic tubes of buffered phosphate and a buffered 2% solution of iodophthalein. The tubes were x-rayed after four days (fig. 5). The opacification reaction occurred only with the bile pigments.

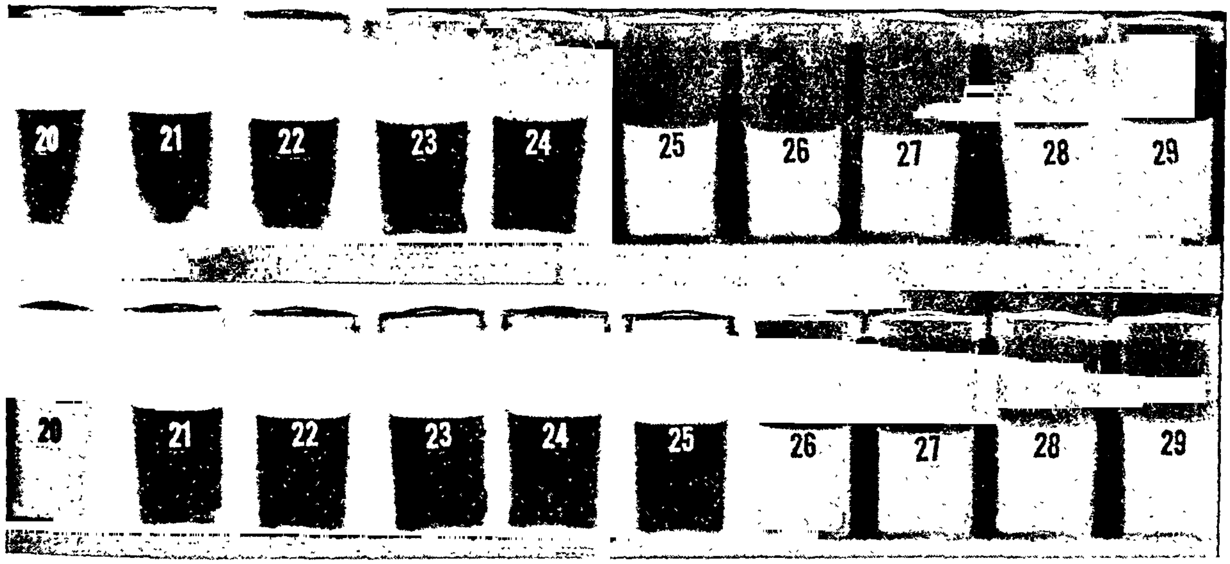

Fig. 4.—Samples of gallstones obtained at surgery or autopsy in unselected cases and immersed in plastic tubes containing buffered 2% solution of iodophthalein sodium: (*top*) immediate x-ray, showing calcified gallstones in 20, 23, and 26, and (*bottom*) x-ray after four days at room temperature, showing opacifying gallstones in 20, 24, 28, and 29.

The following experiments have led us to conclude that a major factor in the opacification phenomenon is a reaction between biliverdin on the surface of the stone and the contrast medium in the bile. Commercial cholesterol, bilirubin, and biliverdin were subjected to the in vitro test for opacifying quality. Samples of each substance were immersed in plastic tubes of buffered phosphate and a buffered 2% solution of iodophthalein. After four days, with these samples kept at room temperature, only the biliverdin was opacified. In addition, nonopacifying infectious cholesterol stones were induced to opacify in vitro after being coated with a layer of biliverdin. There are possibly other unknown substances in the stones which react in this manner with the contrast mediums in addition to biliverdin.

Comment

The hypothesis that the biliverdin in the stone reacts with the contrast medium in the bile, causing opacification of the stone, explains our experimental and clinical observations of the opacification phenomenon. Our knowledge of this reaction, however, is still meager and may belong in the category of speculation.

All pure cholesterol and all infectious cholesterol stones failed to opacify, and all pure pigment stones opacified as would be anticipated. The inconstant opacification of pigmented combined and infectious stones is probably due to the varying surface content of bilirubin and biliverdin in these stones. The high incidence of opacifying stones among bile duct stones which are usually the stasis type is of important clinical significance.

Here, again, there are gaps in our knowledge, but it would seem reasonable that the following sequence of events occurs in the pathogenesis of opacifying bile duct stones: These stones originate in the gallbladder, most commonly as infectious stones, and migrate into the bile ducts. The newly arrived bile duct stone is usually nonopacifying. Usually, the patient with bile duct stones is examined after clinical or subclinical episodes of obstruction and bile stasis. In the presence of extrahepatic biliary obstruction, elevation of the serum biliverdin level has been noted regularly.[7] Bile, regurgitated from the bile ductules into the blood, is the most likely cause of the serum biliverdin level elevation in patients with extrahepatic biliary obstruction. Although the chief pigment in normal human bile is bilirubin,[8] with stasis, bilirubin in the bile is probably oxidized to biliverdin which is deposited on the surface of the bile duct stone, converting the nonopacifying type of infectious duct stone to the opacifying stasis duct stone. Further work is in progress which, we anticipate, will define in greater detail the nature of the opacification reaction.

Summary

Opacifying gallstones precipitate contrast mediums from the bile on their surfaces, after prolonged exposure, with x-ray opacification. The four-day test with use of iopanoic acid (Telepaque), a prolonged preparation for cholecystography, is a useful method for identifying bile duct stones which opacify in over 75% of cases. The test is, probably, the best available method for demonstrating bile duct stones in the presence of jaundice. The method is also helpful in identifying gallbladder stones in problem cases. The gallstone opacification phenomenon has been reproduced in vitro and is due to a reaction between biliverdin on the surfaces of the stones and the contrast medium in the bile.

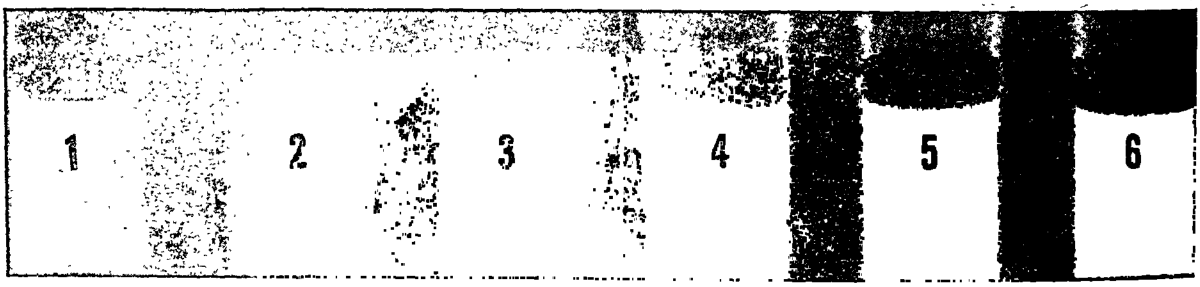

Fig. 5.—X-ray of tubes containing fractionated gallstone (cholesterol, inorganic salts, and bile pigments) immersed in buffered phosphate (*1*, *2*, and *3*) and buffered 2% solution of iodophthalein sodium (*4*, *5*, and *6*). Only bile pigments in *6* are opacified.

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TREATMENT OF MELANOMA BY ISOLATION-PERFUSION TECHNIQUE

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and
Edward T. Krementz, M.D., New Orleans

Metastatic melanoma on the lower extremity has been treated in eight patients by a new technique with use of phenylalanine mustard. An extracorporeal circulation system, consisting of a pump and a disposable oxygenator, was connected either with the common femoral artery and vein or with the external iliac artery and vein so as to achieve vascular isolation of the extremity. This system was then perfused with the phenylalanine mustard for one hour, after which it was flushed out and normal circulation was restored. The characteristic response of cutaneous metastases was a sequence of changes, in that they became blacker and flattened, a crust formed on the surface, and finally the lesion dropped off, leaving a light freckle. Not all melanomas responded in this way, but some lesions regressed strikingly and several disappeared completely. When the vascular isolation of the lower extremity was effective, the amount of phenylalanine mustard used (2 mg. or less per kilogram of body weight) did not seriously depress hematopoesis.

Melanoma is a challenging therapeutic problem because of the peculiar characteristics of growth and spread of these tumors. It is generally agreed that wide surgical excision of the primary lesion is essential, although there is lack of accord as to the necessity for and effectiveness of regional node dissection and for the removal, in continuity, of regional lymphatics.[1] The ultimate results of therapy are difficult to evaluate, because these tumors apparently remain quiescent for long periods of time and metastases may become evident many years after treatment of the primary lesion. Nevertheless, the five-year survival rate, after presumably adequate surgical excision, varies from 20 to 40%.[2]

Radiotherapy of melanoma has proved ineffectual, and the results with systemically administered nitrogen mustard have likewise been unimpressive. As cited by Luck,[3] Bergel and Stock first reported the synthesis of D and L-*p*-di(2-chloroethyl)aminophenylalanine. Haddow, as reported by Bergel and Stock,[4] demonstrated the marked tumorocidal effect of this drug in animals. Working independently, Larionov and associates[5] also reported the synthesis of the same compound and called it sarcolysine. These workers found that sarcolysine caused complete regression of spindle cell sarcoma in rats. Larionov used a mixture of the dextrorotatory and levorotatory forms of the drug, but Bergel and Stock[4] and Luck[3] have shown that the levorotatory form is most active.

In 1957, it occurred to us that the toxic side-effects of this compound and other cancerocidal drugs could be avoided if a tumor-bearing area could be isolated from the general circulation and perfused with these agents. Thus, larger concentrations of the agents might be safely employed. Since there was evidence suggesting that the effects of radiation were potentiated by high oxygen tensions,[6] it was postulated that with use of a heart-lung apparatus for perfusing the tumor-bearing area the oxygen tension of the blood could be increased several times and the propulsive force of the pumping mechanism might produce an adequate distribution of the chemotherapeutic agent throughout the involved part. Techniques were developed in the laboratory for isolation and perfusion of the limbs, pelvis, mid-intestines, and lungs, and maximum safe dosages of nitrogen mustard and phenylalanine mustard were determined.[7] Additional studies also demonstrated that nitrogen mustard remains active in blood for about five minutes and that phenylalanine mustard is active for at least six hours.

Since June, 1957, these techniques have been applied in the treatment of 41 patients with malignant neoplasms of various areas.[8] Among this group were eight patients with melanoma of the lower extremities. This report concerns the techniques of isolation-perfusion in the treatment of melanoma of the lower extremity with use of phenylalanine mustard.

Technique

The extracorporeal circuit used in these studies consisted of a Sigmamotor pump and a disposable bubble oxygenator having a reservoir capacity of 500 cc. The oxygenator is primed with 500 cc. of fresh heparinized blood drawn from the patient immediately prior to operation. Simultaneous replacement of 500 cc. of citrated banked blood maintains the blood volume at a normal level. The common femoral artery and vein, or in some instances the external iliac artery and vein, are exposed through oblique incisions. After occlusion of these vessels proximally, suitable plastic cannulas

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From the Department of Surgery, Tulane University School of Medicine, and the Tulane Surgical Service, Charity Hospital and Touro Infirmary. Dr. Ryan is a Clinical Fellow with the American Cancer Society.

are inserted in a distal direction. To complete vascular isolation of the extremity, an Esmarch bandage is placed at the crotch into the gluteal crease, pulled tightly, and secured to a Steinmann pin inserted into the iliac crest. Perfusion is then begun. The blood is oxygenated with 100% oxygen at a flow rate of 5 liters per minute. When the venous outflow and arterial inflow have been balanced, phenylalanine mustard is injected into the arterial line proximal to the pump to insure adequate mixing. The dose of phenylalanine mustard used varies with the type of diluent used and the mass of the tissue to be perfused. Since this agent is poorly soluble in isotonic sodium chloride solution and distilled water, 2 mg. per kilogram of body weight is used with these diluents. However, phenylalanine mustard is completely soluble in propylene glycol, so only 1.5 mg. per kilogram of body weight is used with this diluent. At the present time, the entire dose of phenylalanine mustard is administered and perfusion is continued for one hour. On completion of perfusion, the venous line is disconnected from the pump and the extremity drained of contaminated blood. Usually about 500 cc. can be removed in this way. Five hundred cubic centimeters of fresh blood is then administered through the arterial cannula and is removed by way of the venous line. The cannulas are then removed, the incisions in the artery and vein are repaired, and the tourniquet is released. Leukocyte and platelet counts are performed every other day after operation to determine the effect of perfusion on hematopoiesis.

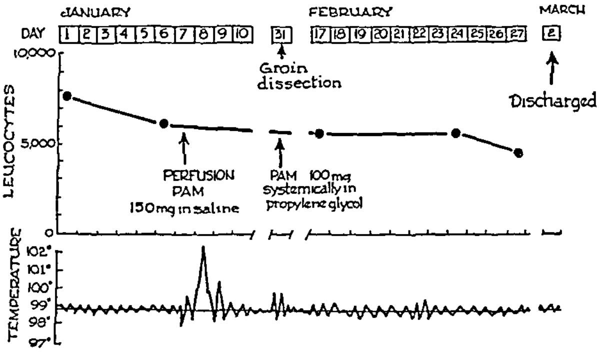

Fig. 1 (*case* 4).—Chart showing leukocyte response to phenylalanine mustard (PAM) administered first by perfusion of lower extremity and later systemically to patient with malignant melanoma.

This technique may be used as adjuvant therapy to surgical excision of the primary lesion or it may precede excision of recurrent melanomas. The following cases illustrate the use of perfusion in both circumstances.

Report of Cases

Case 4.—A 66-year-old man was admitted to Charity Hospital in New Orleans on Jan. 1, 1958, with a history of melanoma of the right heel. The patient had consulted his physician, who had removed the lesion and submitted it for histological examination. Physical examination revealed the site of previous excision of the lesion on the plantar surface of the right heel. There were several large nodes in the right inguinal region but no evidence of cutaneous metastases.

On Jan. 7, perfusion was performed with use of phenylalanine mustard in a dose of 2 mg. per kilogram of body weight dissolved in isotonic sodium chloride solution. After perfusion for 30 minutes, the site of excision on the right heel was widely removed and grafted.

There was no significant alteration in the leukocyte count after perfusion (fig. 1). On Jan. 31, groin dissection was performed and 7 of the 15 nodes removed were positive for neoplastic cells. There was evidence, however, of extensive tumor necrosis in the nodes (fig. 2). Because of the possibility of extension beyond the right lower extremity, a systemic dose of phenylalanine mustard was administered. The subsequent course has been uneventful, except for drainage from the groin incision and persistent edema of the leg; these are gradually subsiding.

Case 7.—A 56-year-old man was admitted to Touro Infirmary on April 30, 1958, with a history of metastatic melanoma, involving the left lower extremity, of two years' duration. In 1949, the patient noted a black mole, which bled freely, on the dorsal surface of the left foot. This was excised and on histological examination proved to be melanoma. Subsequently, he developed enlarged nodes in the left inguinal region but these were not treated. In 1956, a metastasis appeared on the anteromedial aspect of the left thigh and rapidly enlarged.

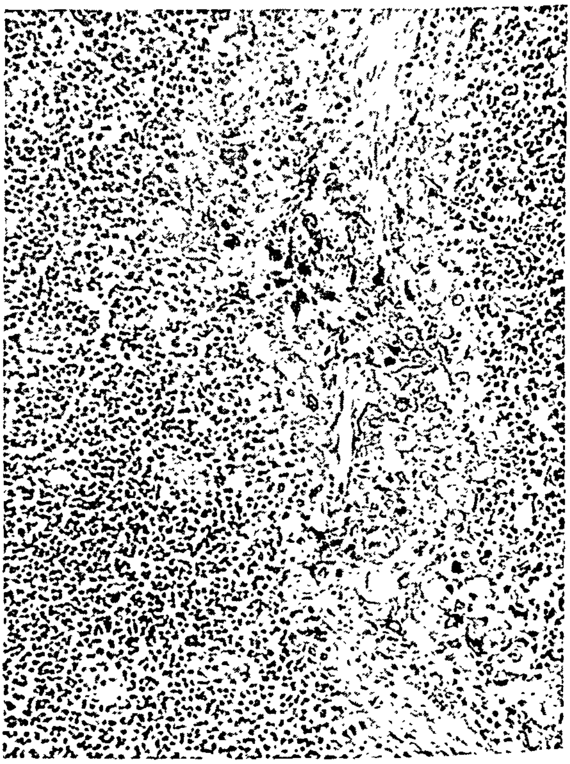

Fig. 2 (case 4).—Photomicrograph of section from inguinal lymph node removed 24 days after perfusion with phenylalanine mustard, showing destruction of metastatic tumor cells.

Physical examination on admission revealed a pale, emaciated man with a metastatic melanoma of the left thigh measuring 30 by 20 by 10 cm. (fig. 3). Its surface was infected and foul-smelling. There were three satellite nodules near the large lesion and a few nodes in the left inguinal region but no evidence of systemic spread of the disease. Biopsy of the lesion revealed poorly differentiated melanoma (fig. 4*A*). After correction of a severe secondary anemia by administration of whole blood, perfusion was carried out on May 5, 1958. Two milligrams per kilogram of body weight of phenylalanine mustard dissolved in propylene glycol was injected into the extracorporeal circuit, and the extremity was perfused through the external iliac artery and vein for one hour. On completion of perfusion, several large lymph nodes along the external iliac vessels were removed en bloc. These subsequently failed to show evidence of melanoma.

The leukocyte count began to decrease on the 10th day after perfusion and fell to 2,400 per cubic millimeter on the 16th day; then it gradually returned to normal (fig. 5). On May 13, the eighth postoperative day, the large metastatic lesion, together with two of the satellite nodules, was widely excised. At the time of removal the large metastasis appeared to be almost completely necrotic, and this was confirmed on histological examination (fig. 4*B*, C, and *D*). However, viable tumor cells were present in some areas. On the 15th postoperative day, May 20, the defect was covered with a split-thickness skin graft. At the time of perfusion the entire extremity was moderately edematous; after perfusion the edema increased. During the first 10 days, the edema was brawny and there was reddish discoloration of the skin over the entire extremity. Gradually, the discoloration turned to brown and the edema subsided. Biopsy of the gastrocnemius muscle at the time of excision of the metastasis revealed marked edema, atrophy, and some hemorrhage but no necrosis of muscle cells. One month after perfusion, two remaining satellite nodules were excised (fig. 4*E* and *F*).

Comment

Among the eight patients with melanoma treated with phenylalanine mustard by the isolation-perfusion technique, six were treated for extensive cutaneous metastases, the primary lesion having been removed previously, and two had the primary lesion removed in conjunction with perfusion of the extremity. There was one patient with a solitary metastasis to the left lung, and the remainder were apparently free of disease outside of the involved extremity.

The first patient with melanoma to be treated by the isolation-perfusion technique has had follow-up studies for more than a year. The cutaneous metastases in this patient have undergone a rather characteristic sequence of changes, in that they become blacker and flatten, a crust forms on the surface, and, finally, the lesion drops off leaving a light freckle. Histologically, these gross changes consist of extensive infiltration with small mononuclear cells which appear to break up the neoplastic cells into islands and, eventually, the entire metastasis is replaced by fibrous connective tissue. During the year since treatment, almost all of the metastatic lesions have undergone these changes and only six of an original 175 cutaneous metastases remain. These have shown no evidence of growth, and apparently the disease is controlled. The urine was positive for melanin prior to perfusion but is now negative. Other patients have exhibited similar changes but follow-up studies have not been done long enough to determine the extent to which the disease is controlled. In one instance, there was striking regression of metastases which were originally from 1 to 3 cm. in diameter. In fact, several of these lesions disappeared entirely. However, after two and one-half months, two of the lesions started to enlarge and showed signs of activity. Perfusion was again done three months after the initial treatment with phenylalanine mustard. Subsequently, most of the residual lesions have been excised.

There was one death in this series. The patient was a 72-year-old man with metastatic melanoma covering almost the entire surface of the right lower extremity and with metastases to the iliac lymph nodes. Perfusion was accomplished through the abdominal aorta and vena cava with phenylalanine mustard used in a dose of 3 mg. per kilogram of body weight. Isolation of the perfused area was not complete, and severe depression of bone marrow became apparent on the seventh day; the patient died on the 15th day.

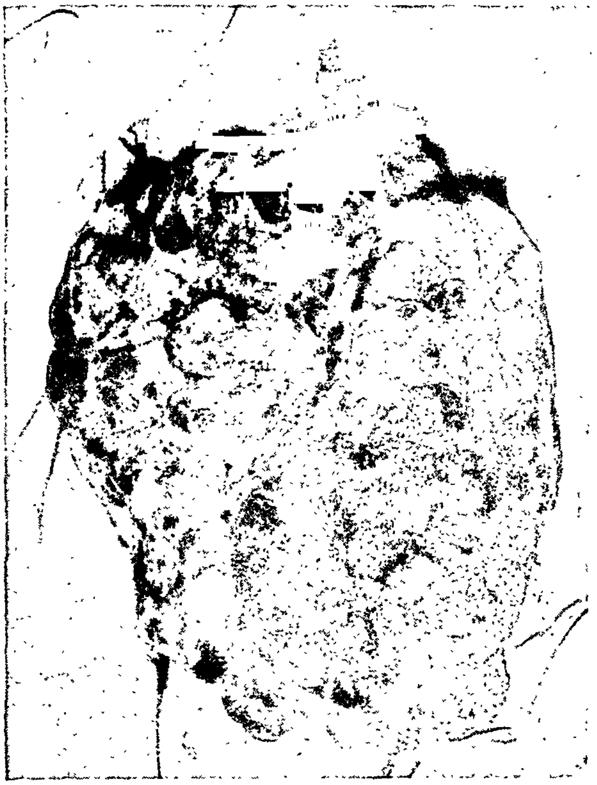

Fig. 3 (case 7).—Metastatic melanoma of left thigh.

Depression of hematopoiesis after perfusion with phenylalanine mustard dissolved in propylene glycol and the absence of this complication when isotonic sodium chloride solution is used as a diluent is not explained. It may be a result of incomplete isolation and/or retention in the tissues of the more completely dissolved phenylalanine mustard.

Evidence, derived largely from the first patient who received perfusion but to a less extent from subsequent patients, suggests that phenylalanine mustard, in addition to destroying neoplastic cells directly, also initiates certain changes which make these cells more susceptible to resistance factors of the host. This assumption is based primarily on the observation that regressive changes within the neoplasm continue long after the drug has become inactive and after the period of acute cellular necrosis resulting from the chemotherapeutic agent has passed.

It is apparent that not all melanomas respond to phenylalanine mustard in the same way and to the same degree. On the other hand, there may be other agents to which melanomas unresponsive to this drug will respond. Thus, there is a need for greater specificity of agents and some means of determining this specificity. Studies are now being conducted to evaluate the feasibility of using tumor transplants to determine the most effective chemotherapeutic agent prior to the use of the isolation-perfusion technique.

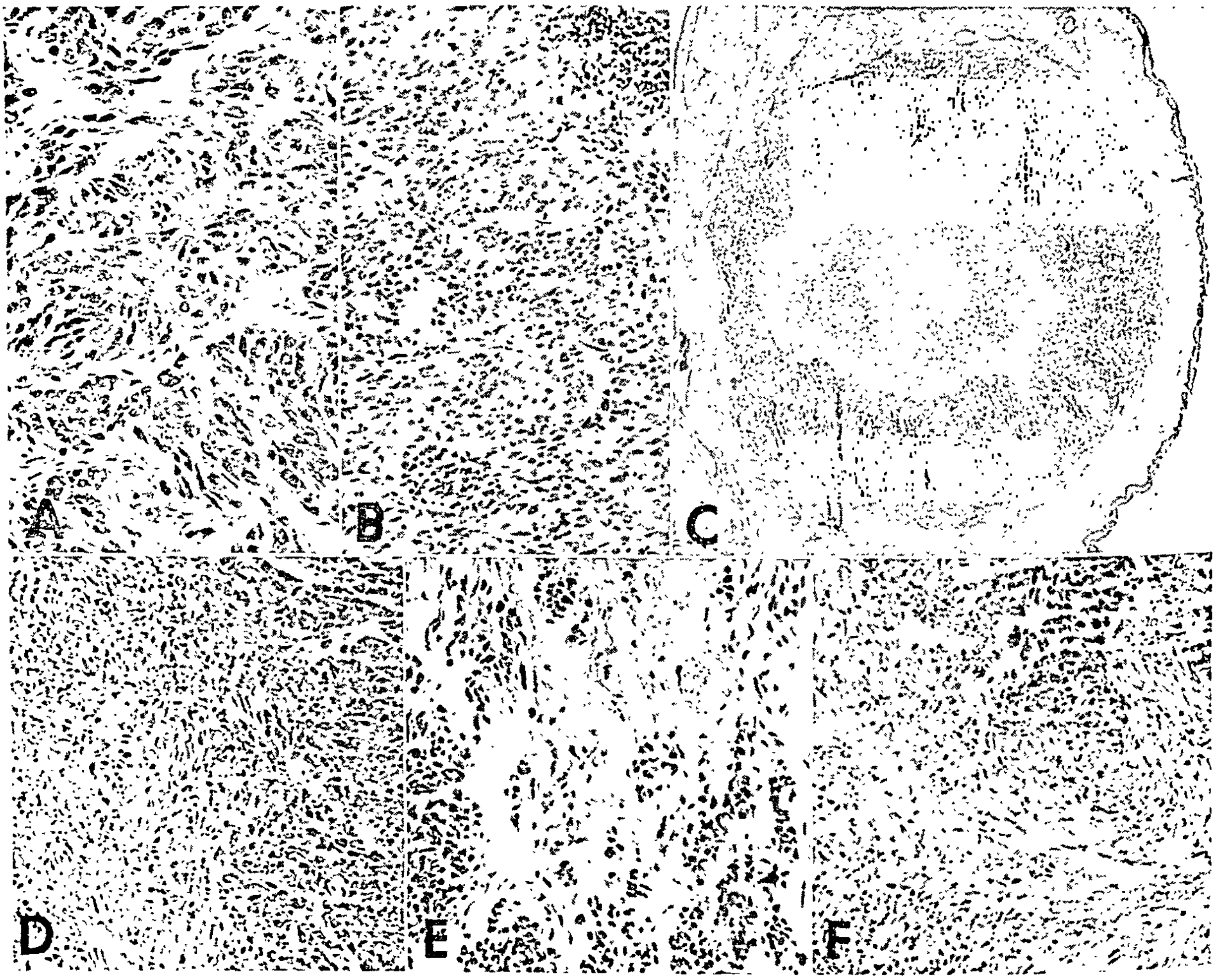

Fig. 4 (case 7).—Photomicrographs of sections from large metastatic lesion of thigh and subcutaneous satellite lesions. *A*, thigh lesion prior to perfusion; *B*, thigh lesion 48 hours after perfusion; *C*, satellite lesion, eight days after perfusion, showing extensive central necrosis; *D*, same lesion with higher magnification, revealing widespread necrosis with scattered areas of viable tumor cells; *E*, satellite lesion one month after perfusion, showing viable cells; and, *F*, also extensive destruction in many areas.

Summary

In order to administer high concentrations of chemotherapeutic agents for the treatment of cancer, a technique of isolating and perfusion of the tumor-bearing area has been developed. Eight patients with malignant melanoma have been treated by this technique. The regression, even disappearance, of neoplastic lesions in these patients indicates that phenylalanine mustard in high concentrations is effective against melanoma.

When the lower extremity was effectively isolated and phenylalanine mustard was administered in a dose not exceeding 2 mg. per kilogram of body weight, serious depression of hematopoiesis did not occur.

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The phenylalanine mustard used in this study was supplied through Dr. D. S. Searle by Burroughs Wellcome Co., Inc., Tuckahoe, N. Y., and Dr. A. Clark Griffin, the M. D. Anderson Hospital and Tumor Institute, Houston, Texas.

The oxygenator used in this study was supplied by Abbott Laboratories, North Chicago, Ill.

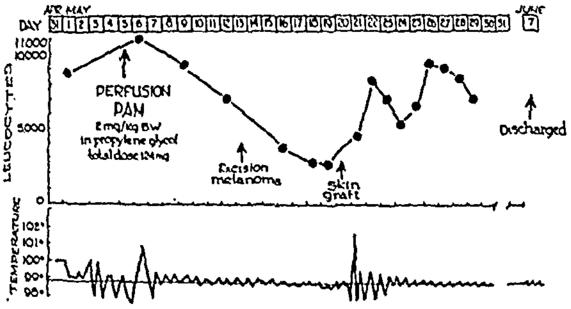

Fig. 5 (case 7).—Chart showing leukocyte response after perfusion of left lower extremity with phenylalanine mustard (PAM), with use of external iliac vessels.

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CLINICAL NOTES

ENDOTRACHEAL TUBE AS A SOURCE OF INFECTION

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Recently reports have appeared in the literature of an alarming increase in hospital infections, many of which are antibiotic resistant and presumably acquired after a patient's admission to the hospital. This is a serious indictment of present-day indiscriminate antibiotic therapy and of our hospitals. Many comprehensive investigations have been conducted in the wards and operating rooms to ascertain the cause of such infections. However, none of these studies has considered the endotracheal tube as a primary source of infection. As a part of the study of wound infections in the Memorial Center for Cancer and Allied Diseases, we undertook to determine if anesthetization equipment, and especially the endotracheal tube, might be a factor in nosocomial infections.

Methods

Initially, we planned to study the anesthetization apparatus as well as the endotracheal tube. However, since the pilot study revealed only common airborne saprophytes from the machine and its parts, the study was focused on the endotracheal tube. Samples from the stock bottles of 5% solutions of hexylcaine (Cyclaine) hydrochloride, used routinely for topical anesthesia, were also cultured at random as the only other source of contamination during anesthesia.

For the past three years in this hospital, routine care of the endotracheal tubes after use has consisted of soaking them in a pan of water containing antiseptic soap with a hexachlorophene content of 0.6 to 0.8% for a period of hours, followed by scrubbing with a similar solution, air drying, and nonsterile storage. Just before use, the tubes have

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From the Memorial Center for Cancer and Allied Diseases.

been washed with this antiseptic soap by the anesthesiologist, rinsed in running tap water, and placed in a sterile towel until used. The endotracheal tube stylet has been treated in the same manner. Using this technique, we prepared two endotracheal tubes at the same time: one was used for intubation of the patient, and the other tube was used for culturing as a preintubation control. Cultures were done on both the control tube and the tube taken from the patient at the end of the procedure by immersion to approximately one-third of their length in thioglycollate broth.

The search for a simple, yet effective, method of sterilizing the endotracheal tube was divided into four phases when failure to obtain sterile controls in this pilot study indicated that our former technique was unsatisfactory. The first phase (13 cases) consisted of an analysis of the above-described methods. In the second series (7 cases), the endotracheal tubes were scrubbed with a brush on the outside for at least 30 seconds with soap containing 0.6-0.8% concentrations of hexachlorophene, followed by rinsing in running tap water. The third series of tubes (20 cases) was prepared by scrubbing with a brush on both the inside and outside for 60 seconds with the soap containing 0.6-0.8% concentrations of hexachlorophene, followed by rinsing in tap water. The fourth series (20 tubes) was treated in the same manner, except for the soap, which was changed to an antiseptic soap with a hexachlorophene content of 3%.

As an integral part of this investigation, cultures were obtained from the nose and throat of all patients studied on arrival in the operating room before any instrumentation was performed.

There were 41 patients in this study, subjected to various operations. Seventeen were subjected to superficial operations on the head and neck, 12 intra-abdominal, 2 thoracic, and 10 intraoral. Follow-up examinations were done for elevated temperature and/or respiratory complications for three days after operation. Two months after the end of the study, all but 7 of the 41 charts were reviewed for evidence of later bacteriological infections.

Results

Of the 41 pairs of endotracheal tubes prepared with the soap containing 0.6-0.8% concentrations of hexachlorophene, only 18 controls, or less than 50%, were sterile. Five of the remaining 23 tubes were contaminated with various nonpathogenic bacteria, and 16 showed various degrees of contamination with staphylococci, streptococci, or both. Only two of these endotracheal tubes were positive for Staphylococcus pyogenes var. aureus.

Of the 20 endotracheal tubes prepared with soap containing a 3% concentration of hexachlorophene, 12 showed no growth, 4 showed Staph. pyogenes var. albus and an antitratum species,[1] and 4 were contaminated in transit to the laboratory (these also showed an antitratum species). (These tubes were prepared in sets of four per day.) The cultures from bottles of 5% solutions of hexylcaine were uniformly sterile.

The nose and throat cultures obtained prior to anesthetization from the 41 patients showed a variety of flora, as would be expected. Eighteen of these patients had a nose or throat culture positive for Staph. pyogenes var. aureus. Eleven of these 18 patients had been admitted to the hospital the afternoon before operation; only 4 patients had been in the hospital for more than two days prior to operation. In addition, one patient showed Klebsiella pneumoniae and four had beta-hemolytic streptococci in the nose or throat. The remainder showed the usual nose and throat flora. Both of the above noted cultures which were positive for Staph. pyogenes var. aureus in the control were used (fortuitously) in intubation of patients whose nose or throat culture contained this organism prior to anesthetization.

Cultures obtained after extubation from the 18 tubes which gave negative findings before use showed a variety of contamination. Except for two contaminations with Proteus species and Aerobacter aerogenes, the organisms found on the extubated tubes had occurred in either the nose or throat of the patients before intubation, as shown by our preinduction cultures, including six instances of contamination with Staph. pyogenes var. aureus.

The bacteriology department records show that only two patients had subsequent bacteriological study; one was for septicemia occurring three months later in a chronically ill, terminal patient, and the other was for a perineal abscess occurring two weeks after surgery. A stitch abscess, not cultured, occurred in one patient.

Eleven patients complained of sore throat or hoarseness which lasted up to two days. Two of the seriously ill patients had minor pulmonary problems in the postoperative period. There were no fatalities in this series. Thus, there was an incidence of wound infection of approximately 5% (2 out of 41) in this series, which is the same as the over-all incidence reported for this hospital in a study of all postoperative wound infections.[1A]

Comment

This hospital, in common with many others, has experienced an increase in the number of antibiotic-resistant infections. The possibility that the endotracheal tube is a source of these infections has been studied in the program initiated to determine the magnitude of the problem and the possible sources of contamination.

Anesthetization equipment has previously been studied from a bacteriological standpoint, but only one report has made note of the endotracheal tube and none has considered this equipment as a potential source of these infections. McDonald and co-workers[2] deliberately contaminated tubes and masks with sputa and known cultures of organisms and then cultured them after washing with five methods: control (no washing), Ivory soap, hexachlorophene soaps (Gamophen and pHisoHex), and green soap. Of these "only pHisoHex produced consistently sterile tubes and masks." Gross[3] found that a five-minute scrub with tincture of benzalkonium (Zephiran) chloride would result in almost complete disappearance of organisms from rebreathing tubes, tracheal catheters, and airways.

Ziegler and Jacoby[4] found the gas machine parts to be heavily contaminated with saprophytes but concluded that transmission of organisms from patient to machine or vice versa was unlikely to occur. Adriani and Rovenstine[5] in 1941 found that organisms were efficiently killed by passage through the soda lime canister. However, Livingstone and associates[6] in 1951 reported one-third of 39 face masks removed from patients with active pulmonary tuberculosis to contain viable tubercle bacilli. This incidence was reduced to 15% by simple washing.

Joseph[7] in 1952 showed the value of the 3% concentration of hexachlorophene in controlling the bacterial count of the rebreathing tubes and bags of anesthetization machines. Pathogenic bacteria were not common, although the incidence is not mentioned in the 18 cases studied.

In our initial experiments, the chimney Y and inspiratory and expiratory tubing were cultured with a swab technique but few organisms were obtained and these were commonly occurring airborne saprophytes. This phase of the experiment was therefore discontinued, and attention was focused on the endotracheal tube.

It is desirable, of course, that any mechanical devices introduced into the patient be sterile. However, the method used to produce this should be simple, reasonably rapid, and without the hazard of chemical irritation which exists when the endotracheal tubes are soaked in certain antiseptics. These requirements are met, with material already on hand in the operating room, by scrubbing with a brush for one minute with an antiseptic soap containing a 3% concentration of hexachlorophene, but not with regularity if the soap contains only 0.6-0.8% concentrations. The topical anesthetic hexylcaine used in this hospital does not serve as a source of extraneous bacteria when administered transtracheally via a sterile syringe and needle.

Staph. pyogenes var. aureus was cultured from the nose and/or throat of 50% (21 of 41) of the patients on arrival in the operating room, along with a variety of other flora, usually after only a one-day stay in the hospital. All organisms cultured from the sterile endotracheal tubes after removal from the patient had been cultured from the nose or throat of the patient before induction of anesthesia. Thus, we have introduced no new bacteria into the patient. However, the possibility exists that a path is provided by the endotracheal tube for the migration of these bacteria from the mouth to the trachea during anesthesia.

Summary

Adequate sterilization of endotracheal tubes can be obtained by scrubbing them with an antiseptic soap containing a 3% concentration of hexachlorophene. Scrubbing with an antiseptic soap containing 0.6 to 0.8% concentrations will produce sterility less than half the time. The 5% solution of hexylcaine (Cyclaine) hydrochloride used for topical anesthesia does not support the growth of bacteria.

In this series, there was a 50% incidence of Staphylococcus pyogenes var. aureus in the nose or throat of patients on arrival in the operating room. Postintubation cultures of the endotracheal tube revealed a variety of flora, all of which were present in the nose and throat of the patient before intubation. Endotracheal intubation with adequately sterilized endotracheal tubes is not a source of nosocomial staphylococcic infections. Endotracheal tubes provide no new organism when washed as described but may permit migration of the oral flora into the trachea.

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Miss Anne Blevins supplied technical assistance in this study.

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TOPICAL USE OF NITROFURAZONE (FURACIN) FOR BACTERIAL DERMATITIDES

EFFECTIVENESS OF THERAPY AND INCIDENCE OF HYPERSENSITIVITY REACTIONS

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Although the topical application of preparations containing nitrofurazone (Furacin) (5-nitro-2-furaldehyde semicarbazone) has been established to be highly effective in the therapy of various bacterial infections of the skin, many dermatologists believe that use of such preparations is attended by a prohibitive rate of hypersensitivity reactions.

Recently our interest in topical therapy with nitrofurazone was rekindled when the application of this substance to chronic leg ulcers, previously resistant to many types of treatment, was attended by marked clearing of the infection and healing of the ulcerations without any adverse reaction. With the stimulus of this clinical situation, an orderly investigation of the efficacy and reactivity of topical treatment with nitrofurazone in a group of dermatological patients was undertaken.

Nitrofurazone is a yellow crystalline compound which decomposes at 227 C and darkens slowly on exposure to light. It is bactericidal in vitro for many bacteria, including the majority of those found in surface infections; its antibacterial spectrum encompasses many gram-negative as well as gram-positive organisms; it is not fungistatic.[1]

Procedure and Evaluation

Three types of preparations used in this clinical study were nitrofurazone soluble dressing, nitrofurazone solution, and an experimental preparation, nitrofurazone cream, with nitrofurazone in an aqueous base containing glycerin, cetyl alcohol, stearic acid, mineral oil, sodium lauryl sulfoacetate, methylparaben, and propylparaben. All three preparations contain 0.2% of nitrofurazone. The soluble dressing and the cream were applied directly to the lesions three times daily, while the solution was usually diluted with one to four parts of water and applied in the form of wet dressings for one hour at a time, three times daily.

These medicaments were used to treat or prevent cutaneous bacterial infections in a total of 212 patients, including private office patients and dispensary patients of the University of Cincinnati dermatological clinics and the Cincinnati Health Department.

The manufacturer[2] of the topical nitrofurazone preparations suggests that these medicaments be applied for only five to seven consecutive days, as it is felt that more prolonged application is usually unnecessary in acute cutaneous bacterial infections and that hypersensitivity reactions are less apt to occur if the medicaments are used for a few days only. These recommendations were followed in this investigation in most cases of acute infections such as impetigo, but the medicaments were applied deliberately for much longer periods of time in many of the patients.

Bacteriological cultures were made from the lesions of 28 patients in this investigation, resulting in isolation of 21 strains of hemolytic Staphylococcus (Micrococcus) pyogenes var. aureus and 2 of Proteus species; five of the cultures were sterile.

Clinical results were classified as (1) satisfactory—infection eradicated in an efficient manner, in the judgment of the clinician, or (when used postoperatively after electrosurgery or dermabrasion of acne scars) infection forestalled without evidence of interference with healing or of hypersensitivity reactions; (2) unsatisfactory—infection not controlled or eradicated in appropriate period of time in the judgment of the clinician; (3) equivocal—not possible to evaluate effect on an infection or lesion; and (4) hypersensitivity or primary irritation reaction.

Clinical Results and Comment

The table shows the results of treatment of the various conditions studied in our 212 patients with each nitrofurazone preparation. As indicated, the majority of patients treated had impetigo or pyoderma. The results of treatment with the cream appeared somewhat better than with the soluble dressing, although the number of patients involved is not statistically significant. In the 92 patients with impetigo and pyoderma (where treatment was usually necessary for only several days or one week at most), there was only one case of hypersensitivity reaction to the cream and none to soluble dress-

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From the Department of Dermatology, College of Medicine, University of Cincinnati; Cincinnati General Hospital; and the Dermatological Clinics of the Cincinnati Health Department.

ing. Of the remaining six reactions, two occurred with use of the cream after dermal electrosurgery and two after application of the cream to infected stasis ulcers. There was one reaction to the soluble dressing in a patient with furunculosis. In the foregoing six patients, the reactions occurred only after somewhat prolonged application of one to several weeks in each instance. The seventh reaction occurred from the application of soluble dressing postoperatively after dermabrasion of acne scars and was observed after only two days' treatment. Patch tests in four of the seven patients confirmed that the reactions were due to nitrofurazone.

Effect of Topical Application of Nitrofurazone in Dermatoses

Diagnosis	Patients, No.	Satisfactory	Unsatisfactory	Equivocal	Reaction
Nitrofurazone Soluble Dressing					
Impetigo	23	18	3	2	..
Pyoderma	15	14	1	..	..
Eczema (infected)	..	..	..	..	..
Dermatitis	9	6	1	2	..
Removal site	18	18	..	..	..
Sycosis vulgaris barbae	4	3	1	..	..
Furunculosis	5	4	1	..	1
Post dermabrasion	3	2	1	..	1
Infected atopic dermatitis	1	1	..	..	..
Scleroderma with ulcer	1	..	1	..	..
Total	79	66(83.5%)	9(11.4%)	4(5.1%)	2(2.5%)
Nitrofurazone Cream					
Impetigo	30	29	1	..	..
Pyoderma	24	21	1	2	1
Eczema (infected)	..	..	..	..	..
Dermatitis	8	6	..	2	..
Removal site	25	23	2	..	2*
Folliculitis	15	13	2	..	..
Acne, pustular	8	5	1	2	..
Stasis ulcer	3	1	2	..	2*
Infected sebaceous cyst	3	3	..	2	..
Pityriasis simplex (faciei)	2	..	..	2	6
Ecthyma	2	2	..	..	..
Furunculosis	2	1	1	..	..
Eczema (nummular)	2	..	2	..	..
Acrodermatitis enteropathica	1	..	1	..	..
External otitis	1	..	1	..	..
Pustular psoriasis	1	..	..	1	..
Herpes zoster	1	..	..	1	..
Total	128	104(81.2%)	14(10.9%)	10(7.9%)	5(4%)
Nitrofurazone Solution					
Infected stasis ulcer	2	2	..	..	..
Infected stasis dermatitis	1	..	..	1	..
Erythema multiforme bullosum	1	1	..	..	..
Monilial stomatitis	1	..	1	..	..
Total	5	3	1	1	..
Grand total	212(100%)	173(81.6%)	24(11.3%)	15(7.1%)	7(3.3%)

* Positive patch tests with 0.2% solution and cream. Negative patch tests with cream base and polyethylene glycol.

Our clinical observations with nitrofurazone soluble dressing, cream, and solution in a group of 212 dermatological patients indicate that these medicaments are effective topical antibacterial agents. Hypersensitivity reactions, for the most part, appear to occur after use of nitrofurazone in lesions overlying a large, active vascular bed (as in stasis ulcers and acne scar removal sites), especially if the medicaments are applied for longer than the recommended five-to-seven-day period. In this connection it should be pointed out that cutaneous absorption and hypersensitivity reactions to topical preparations of almost any type are more prone to occur where the medicaments are applied to abraded areas that overlie such highly vascular sites.

It seems probable that dermatologists may have a somewhat biased concept regarding the incidence of hypersensitivity reactions to topical treatment with nitrofurazone, inasmuch as we are usually called to attend precisely those patients who do exhibit such reactions. Naturally, we do not see the much larger group of patients who do not experience reactions from such treatment and for whom these medicaments are prescribed in almost routine fashion, especially in industrial plants and clinics. It may be of some significance that, although more topical preparations of nitrofurazone were used in 1956 and again in 1957 than ever before, and incidental mentions of nitrofurazone in the clinical literature increased accordingly, relatively few current reports mention the sensitizing tendency of the drug.

Summary

Three different preparations containing nitrofurazone (Furacin) were used topically to treat or prevent bacterial infections in 212 dermatological patients. The clinical results were considered satisfactory in 173 (81.6%) of these, unsatisfactory in 24 (11.3%), and equivocal in 15 (7.1%). Hypersensitivity reactions were observed in only 7 (3.3%) of 212 patients, being confirmed by positive patch tests in 4 of these. Of the seven reactions, six occurred after applications of nitrofurazone had been made over large underlying vascular beds, and usually for a longer period of time than recommended by the manufacturer. Dermatologists' views of the incidence of allergic reactions to topical therapy with nitrofurazone may need revision downward, particularly if such therapy is limited to seven days or less and not applied on surfaces overlying a large vascular bed.

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COUNCIL ON NATIONAL DEFENSE

WELCOME ADDRESS

Harold S. Diehl, M.D., New York

The following papers were presented at the Ninth County Medical Societies Civil Defense Conference held in Chicago, Nov. 8-9, 1958. This annual conference is sponsored by the Council on National Defense of the American Medical Association.

These conferences are planned to inform and otherwise assist medical and health personnel for their respective roles in disasters. Conferees have the opportunity (1) to participate in workshop sessions concerning medical preparedness to cope with disasters, (2) to discuss and exchange information dealing with emergency medical services, (3) to be informed on the availability of pamphlets and articles devoted to the medical and health aspects of civil defense, and (4) to hear outstanding speakers report on appropriate civil defense and disaster topics.

FRANK W. BARTON, Secretary.

As Chairman of the Council on National Defense, I want to add the greetings of our Council to my personal good wishes to all of you attending this conference. The program indicates that the sessions will be most interesting and informative. I congratulate the program committee for obtaining such an array of outstanding speakers to discuss timely and important phases of emergency medical preparedness.

We are particularly pleased that Governor Leo A. Hoegh and members of his staff from the Office of Civil and Defense Mobilization are participating in the program. We are honored to have these distinguished guests. A number of important changes have been made recently in civil defense at the federal government level and I am sure that Governor Hoegh is going to outline these developments for you.

In looking over the program I see that the speakers come from 14 states and the District of Columbia. With but one or two exceptions, I know all of them personally. Most of them are physicians. All of them are dedicated persons—dedicated to promoting medical civil defense preparedness among their colleagues and others in the medical and health field. This is evidence that we have physician leaders in many states who are devoting a great deal of their attention and time to medical civil defense preparedness. It should encourage each of us to return to our own cities and communities and do likewise. Indeed, to meet our responsibilities as physicians, we must expand medical civil defense preparedness to include all members of the medical and health professions in every community.

In sponsoring these yearly County Medical Societies Civil Defense Conferences, the American Medical Association, through the Council on National Defense, wants to encourage the medical profession to participate, individually and collectively, in medical civil defense affairs. This is in keeping with the purposes and objectives of the A. M. A.

In anticipation of the possibility of the United States becoming involved in World War II, more than a year before the Japanese attack on Pearl Harbor the A. M. A. established a Committee on Medical Preparedness. This Committee built up a roster of all physicians in the United States with information as to their special qualifications, their responsibilities in civilian medical practice, and their availability for possible military service. This Committee also recommended the establishment of the Procurement and Assignment Service for Physicians and Dentists to plan for the recruitment of a sufficient number of physicians to meet the needs of the military services with the least possible disruption of essential civilian medical services. It was my privilege to serve as a member of the Directory Board of this Service. Then, in December, 1945, immediately after the termination of World War II, the A. M. A. Board of Trustees established a special committee to study what we today call civil defense. That was five years before the United States had a Federal Civil Defense Program. Dr. Hungate, who is on the program of this meeting, will discuss some of the specific activities and objectives of our Council on National Defense and its Committee on Civil Defense. Therefore, I will not comment on the work or the programs of our Council except to say that we are deeply interested in medical civil defense affairs.

Chairman, Council on National Defense, American Medical Association.

It is not enough, of course, that we are interested. We must interest others. That is one of the profession's responsibilities. Tomorrow the Association's President, Dr. Gunnar Gundersen, will speak about these responsibilities.

I noted with considerable satisfaction that one of the features of the program this year will be reports on the experience gained from three civilian defense test exercises. Such exercises are invaluable to test medical plans and preparations for meeting disasters. Sometimes, also, a real disaster may put these to a test. You recall, I am sure, how the people of Lake Charles, La., were put to the test by hurricane Audrey in 1957. Fortunately, in the communities most severely struck by this hurricane civil defense was well organized and disaster plans well developed. The thousands of hours which civil defense workers of these communities devoted to preparation were invaluable in providing the survivors of hurricane Audrey with essential emergency medical services. However, even with the fine planning and the heroic actions in this natural disaster, much was learned from this experience that will improve their civil defense performance for a possible future emergency. Among other things learned from this experience were that a special civil defense short-wave radio channel was needed, as were more nurses in the civil defense organization, better transportation liaison, less overlap in command, and battalion aid station chests in hospitals to supplement the 200-bed civil defense emergency hospital. Incidentally, this 200-bed emergency hospital unit was put to actual use for the first time in the Lake Charles disaster. Even without the catastrophe of another world war, local physicians may be called upon at any time to provide emergency services such as those which saved many lives in the Lake Charles area. For such emergencies, as well as for the possibility of war, we must be ready.

THE AMERICAN MEDICAL ASSOCIATION CIVIL DEFENSE PROGRAM

Carroll P. Hungate, M.D., Kansas City, Mo.

The Civil Defense Committee of the Council on National Defense directs its activity toward the following specific objectives and projects: The Committee sponsors a one-day session on civil defense and related problems on the Saturday preceding the Annual Meeting of the American Medical Association and a two-day session on civil defense and related problems, annually, in the fall, for county medical societies. It prepares permanent reports of sponsored meetings for state medical associations, county medical societies, and those attending such sessions.

The Committee accomplishes the necessary research for testimony before congressional committees concerned with civil defense. It acts in a liaison capacity between the A. M. A. and national organizations concerned with disaster preparedness. On request, it recommends physicians for membership on advisory committees, private or federal, concerned with civil defense and disaster preparedness. Resolutions are prepared by the Committee for submission to the A. M. A. Board of Trustees concerning matters pertaining to disaster preparedness which require action by organized medicine. The Committee is the contractural agency with federal agencies, on request, for special study projects. It provides a continuous educational program related to disaster preparedness, and, during special civil defense and disaster exercises, it participates in the evaluation of medical disaster planning, equipment, and supplies.

The Committee meets periodically (at least semiannually) in each region in the United States with representatives of state medical associations and women's auxiliaries to these associations. Educational material is prepared by it for state medical associations. It discovers physicians with capability in disaster planning and provides them with an opportunity for national recognition through dissemination of their special work. Finally, it arranges for attendance of members of the medical profession at testing of nuclear weapons in Nevada.

The one-day session on civil defense and related problems, held prior to the Annual Meeting of the A. M. A., brings together the best minds in America for the education of the medical profession. For example, the 1957 session in New York was a milestone in the dissemination of knowledge in the field

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Member, Council on National Defense and Committee on Civil Defense, American Medical Association.

of radiation effects. The county medical society conferences are directed toward the workshop type of meeting where specific problems are considered and an attempt made to solve them. Reports of meetings sponsored by the A. M. A. are prepared by the secretaries of the Council as reference guides for the physicians of the United States and Canada.

In recent years, several committees of Congress have been concerned with civil defense and its budgeting. Testimony by representatives of the American Medical Association requires careful preparation. The influence of organized medicine has been effective in guiding the development of civil defense planning regardless of the political complexion of Washington. In most instances the advice and counsel of the A. M. A. is not only sought but carried out. The present status of the Health Section of OCDM is the result of constant emphasis by the Board of Trustees on the importance of that office.

The A. M. A., through the Civil Defense Committee of the Council on National Defense, has carried on a continuing disaster educational program. Numerous articles on this subject matter have appeared in The Journal. State medical associations have been urged to issue special editions of their state journals devoted to civil defense and to provide at their annual sessions, as a part of the scientific program, lectures or panel discussions on civil defense and disaster. The A. M. A. has encouraged the activity of state civil defense and disaster committees and has recommended that state medical associations include in their annual budgets funds for the expansion of their civil defense program. This budget should provide for travel expenses of state association members to national civil defense and disaster meetings sponsored by the A. M. A. We have recommended that hospital staffs devote one meeting a year to the subject of disaster planning and organization.

The American Medical Association has encouraged special evaluation exercises, such as those held at Fort Mead, Md., and at the Brooke General Hospital, to test the adequacy of civil defense equipment and supplies. The A. M. A. observers have been on hand at special university medical school disaster exercises. Participants in such exercises or those with actual disaster experience have appeared on programs sponsored by the American Medical Association in order to provide first-hand practical data for the profession.

In a liaison role, the A. M. A. has stimulated national associations and societies to appoint civil defense committees at each echelon of their organization and to encourage training of their membership. The inclusion of disaster plans and exercises as a part of hospital accreditation is the result of the initial recommendations of the A. M. A.

In the past year there has been an innovation in the relationship of the Committee on Civil Defense of the Council on National Defense and its state counterparts. The A. M. A. committee has been meeting in the various OCDM regions of the United States. This has brought to the grass roots areas a close association with the parent organization, thus giving a feeling to the A. M. A. membership that we do not sit in an ivory tower.

The success of disaster planning and operation requires the continual infusion of new faces into the program. From time to time, on our trips about the United States, new talent is discovered. These physicians are encouraged to present their thoughts to the profession at large at one of our annually sponsored meetings. Of course their subject matter and manner of presentation must be of the caliber to merit such recognition.

The A. M. A. has used its influence with the Civil Defense Administration and the Atomic Energy Commission to permit physicians and ancillary personnel to attend and actively participate in the medical aspects of nuclear weapons testing at Yucca and Frenchmen's Flats in Nevada. These experiences result in a better understanding of the medical problems associated with modern warfare. They also act as an incentive for greater effort, perseverance, and action by physicians on return to their home towns.

An educational program does not always produce immediate or startling tangible results. The activities of the profession in the field of disaster preparedness has, however, produced a revolution in the United States. Civil defense activity is everywhere. Our population is aware of the Communist threat whether they face up to the realities of the day or not. Progress is made year by year in the proper approach to natural and man-made disasters. Changes in federal and state laws and local ordinances are evidence of the fact. Improved techniques in the management of disasters are seen everywhere.

To properly handle the medical effects of nuclear weapons was, long ago, recognized as the greatest organizational challenge to American medicine in the 20th century. We are meeting this challenge, and our results are reflected in the better handling of natural disasters and new awareness of the effects of radiation in industry, medicine, and research and from atomic sources. The responsibilities imposed upon the medical profession in the atomic age are being met by all of us.

THE FEDERAL CIVIL DEFENSE PROGRAM—OCDM

Leo A. Hoegh, Washington, D. C.

The fact that you are here today is clear evidence that you are dedicated to the proposition that America must live. The challenge that is before all of us, in this hazardous age, is to make certain that our nation and its people survive any disaster that might be directed against us.

It is good to know that you are as deeply interested as I am in the problems of the nuclear age. I know of no group, no profession, that is more dedicated to the cause of civil defense than are you and all the other members of the American Medical Association.

It is a good thing for all of us that you are. It is with you, and all others so strategically situated, that our civil defense effort will succeed or fail. I am sure that you mean to make it succeed.

We at the national level of civil defense and defense mobilization can make all kinds of plans and plan all kinds of actions. Nevertheless, it is you at the local level of civil defense who will be the decisive factor if we are ever attacked.

Your service does not wait until that critical moment, however. Medical societies in all of the nation's communities have long been among the leaders of local planning for civil defense. You have provided strong leadership in planning, organizing, and educating our people. People have a confidence in you that is a priceless asset. We need all of the confidence we can get as we deal with the many intangibles that go to make up a real civil defense.

Militarily, today, we are stronger than we have been in our whole history. We have excellent defensive capabilities, and we have tremendous retaliatory striking power. To make us as strong as we should be, however, we need to match this with an equally strong nonmilitary defense.

If we ever are attacked, it seems quite clear that our cities, our industrial establishments, and our military and atomic energy installations will be battlegrounds. Hence, we must create a total ability to survive, recover, and win such a conflict.

I am not predicting that such an attack will occur. I do not expect one. I do know, and I believe you will agree, that so long as nuclear weapons and fast delivery systems exist in Russian hands such an attack is possible. We must never say "it can't happen here," because history records too many wars that were started by fanatics or zealots. In this age it would be much too easy to push the wrong button.

America must live. It has been the hope of oppressed mankind for 180 years, and it remains today as the shining dream for millions. To live, we must be strong. In creating the kind of strength we must have, it is entirely possible that we could prevent an attack from ever occurring.

Strength is always a deterrent. Even the foolish would hesitate to attack a nation that is prepared to survive and recover.

Where do we find this strength? It can come from the only two elements that are basic to an adequate civil defense: government and people. This is not new to you. It long has been clear that government at all levels must be prepared to maintain control and to direct action in any emergency situation. It is equally clear that the effects of nuclear weapons, such as the possibility of extensive radioactive fall-out, virtually demand that individuals must be prepared to protect themselves and their families, for as much as two weeks, entirely without help from the outside.

A year ago, Mr. Lewis E. Berry, then deputy administrator in the Federal Civil Defense Administration, discussed these responsibilities with you here at some length. Nothing that is basic has changed, but in this year there have been quite a number of developments which are putting real strength in the nation's nonmilitary defense, and it is these developments that I will now discuss.

New Developments

The National Plan.—Two weeks ago we began the distribution of the National Plan for Civil Defense and Defense Mobilization. With a promulgation signed by President Eisenhower, the plan establishes national nonmilitary courses of action both to deter aggression and for national survival in the event of attack.

The plan sets forth the specific mission of each level of government—federal, state, and local—for professional organizations and for the individual citizen. All of the basic civil defense principles and responsibilities for protecting life and property are clearly set forth in this one document.

It creates a civil defense channel of coordination down which instructions will be transmitted and up which requests for assistance will be made. It states our mission clearly: "To protect life and property from the effects of attack by preparing for and by carrying out emergency functions to prevent, minimize, and repair injury and damage," and the mobilization of resources and production. It sets forth the functions and, step by step, how the mission is to be accomplished and by whom.

Director, Office of Civil and Defense Mobilization.

Simultaneously we have been issuing a "Summary of Annexes" so that all who have responsibilities under the plan will know in just which forthcoming annex the details of his own mission will be spelled out. These annexes are being prepared right now, and we expect to issue them as rapidly as each is completed and approved by all concerned.

A number of them will be of interest to you, particularly the National Medical and Health Plan, which will be Annex 18. This is the responsibility of the U. S. Public Health Service, by delegation to the Department of Health, Education, and Welfare. You will be interested to know, I am sure, that Dr. Robert Leslie Smith, who has been assistant administrator for Health and Medical Affairs of FCDA, now has been recalled by the Public Health Service to have a direct responsibility for carrying out the delegated functions.

Other annexes that you will find of interest include the National Radiological Defense Plan, the National Biological and Chemical Warfare Defense Plan, the National Food Plan, and Mass Care and Assistance. In all, there will be 40 annexes, covering in detail all aspects of civil defense and defense mobilization—in short, the nation's passive or nonmilitary defense.

Reorganization Plan No. 1.—Such a comprehensive document could not have been issued six months ago. Necessary to its perfection was congressional approval of President Eisenhower's Reorganization Plan No. 1 of 1958, which became effective last July 1.

This plan merged the Federal Civil Defense Administration and the Office of Defense Mobilization as the Office of Civil and Defense Mobilization in the executive office of the President.

By the President's executive order putting this into effect, all of the nonmilitary responsibilities of the federal government were laid directly in the hands of the President, who thus takes direct charge of the nation's total defenses. He has delegated to me those responsibilities that lie outside the military area.

This has been a tremendously important step for the cause of civil defense and defense mobilization. It has given great new strength and stature, a proper standing in the federal government, to the mission for which we must answer to the President.

Public Law 606.—In a different direction, Congress took another action to strengthen civil defense when it unanimously passed H. R. 7576, which now is known as Public Law 606. This alters the whole federal-state relationship and changes a completely outmoded concept under which Congress held for eight years that civil defense was primarily the responsibility of the states and their political subdivisions.

Now the basic law under which we operate forthrightly declares that civil defense is a joint federal-state-local responsibility. It gives meaning to that relationship when it authorizes us at the federal level to help the states and cities with their administrative and personnel costs. It also authorizes us to help pay training and personal equipment costs at these levels and a large program for the purchase and distribution of radiological measuring instruments.

It is my hope that, early in the new year, we will have Public Law 606 in effective operation, thus putting new sinews in state and local organizations. Passage of the act came so late in the last session of Congress that there was insufficient time to obtain the funds that it authorized, but congressional leaders have invited me to return in January to ask for the needed funds.

The National Shelter Policy.—As medical men, you will be interested to know, too, that I intend at the same time to ask for funds to put into effect the National Shelter Policy adopted by the Administration last May. This policy sets forth five courses of action, which I will review briefly: 1. Intensive education of every American on the possible effects of nuclear attack and the actions he and his government can take to minimize them. This means a sharp stepping up of our educational and informational programs. 2. Making surveys of existing structures to determine their shelter capabilities and what must be done to bring them to standard. 3. Accelerating research to show how shelter may best be incorporated in both existing and new structures, to improve shelter designs, and to reduce costs. 4. Construction of a limited number of prototype shelters for varied geographical and climatic areas, insuring that they have practical peacetime use as well. 5. Setting federal example by incorporating fall-out shelters in federal buildings hereafter designed, as in indispensable stimulation of state and local governments and to private investment. I have issued a general order to all federal departments and agencies to make this provision effective. In addition to these new developments of the last year, there are three continuing programs on which we are putting more and more emphasis.

Continuing Programs

Continuity of Government.—Government must continue without interruption, and with full force and effect, under any conceivable emergency. The survival of the nation in no small measure depends upon the ability of federal, state, and local governments to carry out their responsibilities in the event of nuclear attack.

To be certain of the ability to continue functioning, all governments must take these four steps: (1) establish automatic lines of succession for all key officials, appointed or elected, and covering all branches of government—legislative, executive, and judicial; (2) preserve, and hold at alternate sites, all of those records necessary for the orderly operation of government and for the protection of individual rights; (3) establish emergency locations from which the governments of states, counties, and cities can continue to function under adverse conditions; and (4) provide for the emergency use of all government personnel, facilities, and equipment.

This program has the support of governments at all levels, and legislation and constitutional amendments to make it effective will be before 44 state legislatures that are convening in January.

Radiologic Defense.—Since radioactive fall-out from a nuclear attack could become a nationwide problem, we are working as rapidly as possible to develop a nationwide capability of detecting and measuring radiation. We are taking four actions simultaneously: We are providing instruments and training to state and local civil defense officials. We are providing both instruments and training for the personnel of 900 federal aviation agency and weather bureau stations, giving us fixed monitoring capability. We are providing kits of training and monitoring instruments this year to 15,000 high schools, or about half of the nation's total. We expect to provide them for the other half in the next two years and, as a result, to train about 2 million students a year. Through schools and traveling teams, we are training science teachers and other instructors who, in turn, can teach many more individuals in this most important service which someday might be needed at almost every community in the nation.

Survival Planning.—Operational survival plans have been completed in 38 states and many metropolitan target areas, and work is being pushed to complete the rest of a total of 195 plans by Jan. 1, 1959. When these are finished, the states will have detailed operational plans to deal with emergency situations. These plans will cover more than 97% of the population.

All of these plans will be completely linked to the National Plan for Civil Defense and Defense Mobilization. Together, they will give solid substance to our nonmilitary defense from a governmental standpoint.

Comment

I realize that, as deeply interested in civil defense as you are, you very well may be aware of all of these developments of the last 12 months, but I felt that a review of them would be in order, especially as they relate to each other to form the substance of our over-all program.

We must keep firmly in mind, at all times, that it takes more than government to create a strong civil defense. Equally important are people and their own personal preparations to survive. This is basic. So much of the country could be affected by a nuclear attack that no one would be able to help anyone else.

That is why we say that every American must know these five things: warning signals and what they mean; your own community plan for emergency action, protection from radioactive fall-out, first aid and home emergency preparedness, and the use of Conelrad—640 or 1240 on your radio dial—for official directions.

These are the minimum requirements on the individual, with whom all civil defense would start if the United States suffered an attack. The national plan clearly sets forth that individuals and families will be expected to exist on personal stocks of survival items in homes and shelter areas for two weeks. They must prepare their own shelter from fall-out radiation. It is in this area of personal preparation that we must devote intensive educational effort, and we are going to do it.

Conclusions

For a long time, a severe handicap to the development of an effective civil defense has been represented by the two comments, "It can't happen here," or, "If it does happen, there's nothing we can do about it." We know it can happen—as long as nuclear weapons and fast delivery systems exist. Now we also know what can be done about the threat. Our plans and programs are sound. They will enable the United States to survive an attack, to recover, and to go on to win.

The pessimist, the defeatist, the cynic can always present the dramatic. For instance, a recent report states that in case of a nuclear attack there would be 160 million casualties. Nothing could be further from the truth than such a statement.

The report is based on three false assumptions: (1) that everyone is outside and will remain outside for two weeks, (2) that there is no civil defense capability, and (3) that the enemy is free to hit all probable targets. Such a report contributes to the philosophy that "nothing can be done about it."

The people of the United States have always had a fierce will to win and to remain free and independent. With the help and leadership of such dedicated men as you here, I feel certain that we can guide that spirit into the coöperative work of creating a civil defense that is worthy of the United States, which has never settled for anything less than the best.

NATIONAL MEDICAL PREPAREDNESS

W. Palmer Dearing, M.D., Washington, D. C.

President Eisenhower, in addressing the National Defense Executive Reserve Conference last November, said that planning is everything but when the emergency actually occurs plans go out the window. "The definition of 'emergency,'" he said, "is that it is unexpected, therefore, it is not going to happen the way you are planning."

This paradox was startling to some of us who have devoted our energies to mobilization and civil defense planning. Webster defines a paradox as "an assertion or sentiment seemingly contradictory, or opposed to common sense, but that yet may be true in fact." As we continue to try to do our part to help achieve the posture of total defense which Lewis Berry spoke to you about a year ago, we appreciate more and more the cogency of the President's paradox.

It expresses on the one hand the virtue and indeed the necessity for undergoing the planning process—not once, not twice, but continually—to develop the means, the organization, the state of mind, and habits of thought and action which are essential to effective performance. On the other hand, it expresses the fallacy of becoming wedded to static plans which are sure to become outdated and hampering. A real situation will never conform to the assumptions on which our best plans are based.

In discussing national preparedness, I should like to stress the importance of our state of mind—our habits of thought. I should like also to report some developments which should enable us to carry forward better the serious work to which you have so long been dedicated—the work of planning, training, and organizing for the total defense of the United States.

Education and Training Problem

The importance of state of mind is illustrated by a story which Dr. Elmer Hess, chairman of the Health Resources Advisory Committee, tells of a conversation with his barber. This man, described by Dr. Hess as having considerable intelligence, was voicing the fatalism which many of our fellow citizens adopt as an excuse for inaction and lack of interest in civil defense. He said that if a bomb hits, that is it! Dr. Hess inquired where he lived, and he stated that his home was some 35 miles outside of Erie, Pa. When Dr. Hess pointed out that if a bomb struck Erie, his family could very well be saved if they had made some simple preparations, the barber asked, "Why doesn't the government tell us these things?" Well, of course, the government has been trying to "tell us these things," but education is a slow continuing process in which we must all participate.

The awesomeness of modern weapons so overwhelms us that we tend to concentrate on their destructiveness. We would better follow the principle which has proved so effective in rehabilitation of the injured individual: concentrate on what you have left and not on what you have lost. Of course, there will be losses, but surviving resources—people, doctors, supplies, crops, raw materials, and productivity—are the things on which we must concentrate. Further, let us keep reminding ourselves that it is preparation of our people and our profession for survival which is, along with our preparation for military defense and retaliation, the third great deterrent to an attack.

The importance we in the Office of Civil and Defense Mobilization attach to our "state of mind" is manifest. One of Governor Leo A. Hoegh's first organizational moves after the consolidation last July was to make training and education one of the major branches of the new agency by designating one of his three assistant directors for that responsibility.

Our health professions are founded upon education. We have recognized, moreover, that health progress requires continuing education, so we welcome the impetus that this decision will give the entire health program.

To be sure, we intend that federal-level responsibility for purely technical training in the health field will be delegated, along with other operational responsibilities, to the U. S. Public Health Service. Education and training in health matters, however, must be an integral part of the general education effort.

The health professions have an important responsibility to participate in the education of the general public for disaster. We know that individuals, families, and larger population groups will be on their own for varied periods of time after a major attack. The entire population will be short of medical supplies and facilities in varying degrees. Widespread health education, including first aid and home nursing training, is a fundamental step toward survival, and we in the health professions have the teaching job to do.

Health Services Problem

Another development which denotes some progress is the trend in our thinking toward considering the health services problem in a survival situation as a unity. One manifestation of this trend is the administrative decision, with which you are quite

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Director of Health Services, Office of Civil and Defense Mobilization.

familiar, to make the delegation of operational responsibility to the Public Health Service comprehensive instead of piecemeal. The advance in our thinking which I want to stress to you, however, grows largely from our annual exercise—Operation Alert 1958.

This exercise was the most successful we have had. Instead of trying to do the whole job in a week, as heretofore, we conducted the exercise in three phases: (1) the civil defense phase in May, when the states and communities tested their capabilities for taking action; (2) the federal action phase in July, when the federal agencies devoted a week to dealing with the problems which had arisen in the states as a result of the effects of the simulated attack upon the national resources and capabilities; and (3) the seminar phase in September, when the entire results were analyzed at the Cabinet level and reviewed by the President and when certain courses of action were adopted.

In the health field, we hammered out the concept of this unity of the health problem to which I have referred. Rather than thinking of the job in segments, such as casualty care, medical service to the uninjured, and environmental sanitation, we are now talking about health care of the surviving population. Rather than setting casualties apart from the uninjured population in considering priorities for health services, we are recognizing that a health problem, whether it be of personal injury or of public health hazard and whether it resulted from direct enemy action or from "natural causes," has the same effect on people.

In the course of this exercise, we have further refined the priorities which Dr. Van Sandt presented here at your conference a year ago. Here is how we presently state the priorities for health care: (1) individuals whose lives are endangered by injuries or sickness but whose chances of recovery with hospital treatment are good, with treatment confined initially to those procedures which are essential in order to save life; (2) pregnant women, with outpatient treatment for normal pregnancies and hospitalization for obstetric emergencies; (3) casualties and noncasualty sick persons whose injuries do not threaten life, with outpatient treatment only or self help; and (4) persons with cases of such gravity that extensive treatment is unlikely to save life.

I think the important thing, however, is not in the precise terms used today or next year but in the pattern of thought—the state of mind—which is trained to recognize the need for priorities and, therefore, is prepared to establish them to fit the situation that exists.

Obviously, the fragmentation of our society which would result from a massive nuclear attack upon the United States would mean that uniform national priorities could not be implemented, even if they might be desirable. The administration of survival health services, therefore, must depend on physicians and other health personnel trained to deal with these new problems of priorities and shortages and, in many cases, to advise the top governmental authority of an area of the requirements that must be imposed.

Metropolitan Area Problem

A third development of interest to the medical profession is the progress in dealing with metropolitan area problems. The metropolitan area has been a knotty problem since long before I began to wrestle with it in civil defense of World War II. Chicago-Gary, St. Louis-East St. Louis, New York City area complex, Washington, D. C.-Virginia-Maryland, and Philadelphia-Camden are well recognized interstate problems. But, a new phenomenon "urban sprawl" is plaguing every large metropolitan area, even if state lines are not involved. The assistant secretary of the Department of Health, Education, and Welfare, Elliott Richardson, in addressing the American Public Health Association last week stated that "'urban sprawl' featured by outward migration from the central city has created particularly an acute problem in the planning of hospital services." The problems of hospitals in this respect are insignificant compared to those of organizing for civil defense and mobilization. Questions of political jurisdiction, financing, and sometimes just plain old prestige and who is to be in charge are just as acute in intrastate metropolitan areas as they are when state lines are involved.

An important new tool for dealing with this problem is the provision in our civil defense amendments of 1958 for giving federal assistance directly to metropolitan area authorities as well as to states for administrative expenses of civil defense. This would include organization and equipment of health services and training of health personnel. This availability of federal assistance should provide real stimulation for the political units to get together.

This will take time, however, and there is an experience of one of you which may point the way toward medical service organization without waiting for political organization. I refer to the experience in Kansas City area as reported by Dr. Carroll Hungate. Our fire departments, almost without exception, have had long-standing arrangements for collaboration and "covering-in" across political boundaries and they have the communications to support effective operation. Dr. Hungate reports that the health services in the Kansas City area have built upon this system and have based their organization upon the metropolitan area fire department system without waiting for "treaties" between Kansas City, Kan., Kansas City, Mo., and adjacent areas.

We are proud of the professional ties in the health world which transcend political boundaries. Here is a practical application to a real situation developed by the initiative of the health profession building upon these ties.

Summary

Three developments denote progress in developing the "state of mind" which we in the health professions must acquire if we are to organize and train for the health survival job. First is the decision in the Office of Civil and Defense Mobilization to increase our emphasis on education and training. Second is our progress toward recognition of the unity of the health survival job both by making a comprehensive delegation of operational responsibility to the Public Health Service and by thinking of our job as health care of the surviving population rather than as a compartmented one. Third is our progress in dealing with the metropolitan area problem which has continued to be one of the thorniest which confronts us. We are moving ahead, and this Ninth Annual Conference of the County Medical Societies Civil Defense Organization is an important milepost.

CHEMICAL AND BIOLOGICAL WARFARE

Paul A. Lindquist, M.D., Battle Creek, Mich.

I would like to start with two definitions defining chemical warfare and biological warfare from a civil defense point of view. Chemical warfare is the intentional use of toxic chemicals to kill or confuse man. Biological warfare is the intentional use of living organisms or their toxic products to produce death, disability, or damage to man, animals, or crops. Note that both chemical and biological warfare are concerned only with living things. These two types of warfare have frequently been called unconventional warfare. They have nothing whatsoever to do with conventional weapons which cause physical destruction not only of humans but of equipment and facilities.

Nuclear and thermonuclear bombs are conventional weapons if we consider the blast and heat effects. Fall-out, however, is in a sense an unconventional weapon since it adversely affects only living things. Chemical and biological weapons or agents are far more flexible than fall-out and offer a wide spectrum of effects. In the case of chemical warfare agents, we have a whole series running from such tear gases as bromoacetophenon, through such lung irritants as phosgene and such vesicants as mustard, to the newer and highly lethal anticholinesterase agents commonly known as nerve gases.

In the field of biological warfare agents we may consider bacteria, viruses, rickettsias, protozoa, and toxins. These in turn vary greatly in their infectivity and in the resulting mortality rate. For example, Rickettsia burneti (Coxiella burnetii), the organism which produces Q fever, has a high infectivity but one would not expect many fatalities. On the other hand, the yellow fever virus and Bacillus anthracis cause a high incidence of death. Between these extremes, there are many variations. Biological warfare agents may also be delivered by different means. Aerosols may be very effective, as well as vectors.

Background

The use of chlorine as a chemical warfare agent was proposed in the early days of the Civil War for use by Northern troops against entrenched Confederate troops. It was not then practical, since the production of chlorine was extremely limited. It was not until a large chemical industry had been built up that toxic chemicals could be used effectively in sufficient quantity in combat.

At the outbreak of World War I, Germany controlled the chemical industry. It is not surprising, therefore, that on April 21, 1915, the Germans released large quantities of chlorine against unprotected allied troops. It was a surprise attack launched early in the morning under favorable meteorological conditions. It resulted in 5,000 casualties and the complete demoralization of 15,000 troops.

In first using chemical warfare agents, Germany did not actually break the Hague Agreement of 1899, since this agreement specifically limited the signatories to abstain from using toxic chemicals "in projectiles." The Germans had used static cylinders. Later the same year, the Germans used phosgene. Both of these agents are lung irritants, and eventually protection was developed through

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Acting Deputy Director, Health Services, Office of Civil and Defense Mobilization.

simple gas masks. To overcome this protection, the central powers launched, in July, 1917, a mustard gas attack which circumvented the mask by penetrating through the skin. In the first three weeks, the Allies suffered 14,000 casualties and 500 deaths. It has been estimated that gas warfare alone during World War I caused 1,200,000 casualties, of which 400,000 were due to mustard.

During World War II the Germans developed another type of toxic chemical, which was neither a lung irritant nor a vesicant but an anticholinesterase agent which attacks the central nervous system. What these agents were was entirely unknown to the Allies until depots containing them were discovered by American, British, and Russian forces. These agents are today considered a possible serious threat to the United States.

Physiologically, these nerve gases inhibit the production of cholinesterase, thus permitting the unrestricted production of acetylcholine with subsequent uncontrolled muscular activity. The only acceptable therapy for nerve gas casualties is the rapid injection of atropine. In severe cases, atropine alone is ineffective and artificial respiration is essential. To illustrate the high toxicity of one of these nerve gases, I might point out that hydrogen cyanide would have to be inhaled at a concentration of 5,000 mg. per cubic meter for one minute to cause 50% casualties. On the other hand, a nerve gas would require 100 mg. per cubic meter for the same length of time to produce the same results.

Not too much is known about biological warfare agents in military operations; however, Dr. Fothergill, in *Military Medicine*, July, 1958, stated, "Infectious disease has often been the critical factor in the outcome of a military campaign." For example, bubonic plague is said to have stopped the Crusaders at the gates of Jerusalem; dysentery probably caused more casualties in Napoleon's Grand Army than enemy firearms; typhoid and the dysenteries played havoc in the Boer and Spanish American Wars; typhus prevented the Germans from carrying through their Balkan campaign in World War I; and in World War II scrub typhus caused 7,000 casualties in the southwest Pacific. In the Korean war, encephalitis B (Japanese type) and hemorrhagic fever were serious medical problems. Little can be said of the intentional use of pathogenic organisms or their toxic products; however, it may be noted that the Germans in World War I are said to have infected horses in the United States destined for the Rumanian Cavalry with glanders. In World War II, German occupation troops stationed in eastern Europe are believed to have been intentionally infected with pathogenic organisms. So much for the brief background on chemical and biological warfare.

Future Uses

What are the Russian interests in these two types of weapons? In January, 1957, Defense Minister Zhukov stated before the Communist Party Congress: "The USSR is rebuilding its Armed Forces on the basic assumption that the means and forms of future war will differ in many respects from past wars. We will see the mass use of air power, various types of missiles, and means of mass destruction like nuclear, chemical, and biological weapons."

There was an interesting article published in *Military Medicine* and *Pharmaceutical Review* (Yugoslavia) by Col. Adam Milkovich in the November-December, 1956, issue. After discussing chemical and biological warfare, the colonel states, "There is less knowledge, less talk, less writing, less thinking about them, and therefore, there is less work done in preparation of defensive measures. The main reason, however, for this is not that biological weapons have never been used in war, but that the use of them has never been detected as was the case with atomic and chemical weapons." Later the colonel states, "From results of comparative studies of losses of life from conventional weapons, war poisons and atomic weapons, on the one hand, and losses from biological weapons on the other, it is believed today that a biological war would have the greatest effect of all." In closing, he states: "Present experience has shown that no special significance would be attached to international decisions on this matter and that it is practically impossible to control either the preparation or the use of biological weapons in wartime."

Russian posters have indicated an interest in chemical and biological warfare. When one speaks of delivery of chemical or biological warfare agents in aerosol form, one usually thinks of small-area coverage. However, one poster shows the travel of a cloud of fluorescent particles released from a ship traveling some 10 miles offshore under selected meteorological conditions. (Slides of this and another poster were shown by Dr. Leroy D. Fothergill before the A. M. A. Medical Civil Defense Conference in San Francisco on June 21, 1958). The particles per liter should be multiplied by a breathing rate of 15 liters per minute to indicate the approximate total inhalated dose. However, in 1950, a somewhat smaller test was run with use of Bacillus globigii.

According to Dr. Fothergill, "A satisfactory cloud was produced even though these nozzles were only about 5% efficient in producing an initial cloud of particles in the size range of one to five microns. In this test, 130 gallons of suspension containing 7.2×10^9 organisms per liter or a total of approximately 3.54×10^{15} spores was aerosolized." This represents a total aerosol cloud of approximately 3½ million billion spores. This aerosol was sprayed from the rear deck of a small naval vessel cruising about two miles offshore and vertical to an on-shore breeze. Spraying continued along a two-mile course.

The maximum distance of the farthest sampling station was 23 miles from the source, and it can be seen from the isopleths that approximately 100 square miles was covered by the sampling area. Dr. Fothergill believes that it is quite likely that even a greater area was covered, particularly downwind. Samples were taken at various levels to obtain the vertical profile of the cloud. The dosages to persons breathing at a rate of 15 liters per minute for two hours were, first floor, 3,440, 9th floor, 4,500, and 15th floor, 562. It would appear, therefore, that height above the ground in most habitable buildings will not provide protection.

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CALIFORNIA CPX—MEDICAL AND WELFARE SERVICES

Frank F. Schade, M.D., Los Angeles

How well can we expect our plans to function? Many methods and techniques for testing have been used in as many places across the United States from the annual Operation Alert to local tests and drills. We are all in agreement that increasing emphasis must be placed upon the capabilities and preparation of the support areas, to which the attacked cities must look for help. These areas are the least prepared to give the required support because of their very limited resources of personnel, facilities, supplies, and equipment.

Methods

A test was devised for the support areas, with two purposes in mind, based upon the premise of an assumed situation of strategic evacuation—no casualties. The first objective was to determine the total medical potential of the support areas of the southern part of the state, known as Region 1. The second was to know if there was any duplication of intention to use certain facilities, such as schools and other large buildings. Welfare is the other service that would have need of buildings and other facilities of the type required by the Medical and Health Service. It was therefore decided to have a joint exercise with Welfare Service, which would also give workers in that section an opportunity to critically appraise their capabilities, as well as provide means of determining and adjusting any conflicts between the two services.

We are interested in thoroughness and accuracy, so there was no narrowly restricted time limit, which is one of the criticisms of the usual CPX. The way it was devised, those participating got training in technical and administrative procedures as well as some actual field work. Fact sheets were prepared, outlining the objectives of the exercise and giving much basic factual information, such as normal expectancy rates for hospitalization per 1,000 population, birth rates, number of women in the last month of pregnancy, death rates, communicable disease rates, and average number of injuries. Guides for the selection and use of buildings for hospitals were also furnished, based upon 60 sq. ft. per patient plus 10,000 sq. ft. for such things as operating rooms, laboratories, pharmacy, central supply, x-ray facilities, kitchens and mess areas, administration, triage, and storage. There were a number of data work sheets, covering hospitalization (two sheets), first-aid stations, staff personnel, supplies and equipment, and public health activities.

The field work consisted of either going over architects' floor plans or actually measuring buildings to determine available square footage of space. Part of the technical training consisted of planning actual hospital layouts in selected buildings, such as high schools or junior colleges. There also was training in personnel requirements, estimating needs and balancing them against actual known numbers available. Further technical training, that also combined field work, was to be had in the public health section of the exercise. In the personnel and supply sections, provision was made to request reinforcements from the next higher echelon, which provided for some much-needed communications and additional administrative training.

Over-all, large-scale master plans are essential to the success of our disaster services, just as in military planning. However, there cannot be any degree of success unless the basic units can perform efficiently. These units are the operational subareas, the individual small communities, and the component sections of the larger cities. This exercise was directed primarily to the operational subareas and provided for the collection and evaluation of all of the above mentioned data, based upon previously

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Chief, Medical and Health Section, Los Angeles County and Cities Civil Defense Planning Board.

furnished quotas of evacuees. The operational subareas then forwarded their reports, along with requests for reinforcement, to the next higher echelon, where they were consolidated. Each level was to attempt to take care of the situation if at all possible before requesting assistance from the next higher level. In this way there was participation, of differing types, at all levels in the chain of coordination. To clarify this terminology, it should be explained that for disaster purposes California is divided into three regions. The region is in turn divided into several sectors, each one composed of several counties. The next lower level is the operational area, which is usually a county. Because of size, population, and the political subdivision complex, Los Angeles County is divided into seven operational areas. The larger cities in turn are broken down into subareas. The smaller community is an entity but corresponds to subareas as far as organization is concerned. Every level, from the individual community or subarea to the region, is given great latitude in operational activity, with the objective of attaining the utmost in autonomy. Every level does its best to handle the situation before calling upon its next higher echelon for help. This makes for a flexible system that can be used for anything from a relatively minor local occurrence to a major catastrophe.

The requirements for the exercise are briefly outlined from the material submitted to those participating: (1) provide medical facilities for patients arriving from critical target areas; (2) determine medical health problems and case loads among the normal population and among the evacuees; (3) determine the sanitation aspects of refugee care; (4) designate facilities for use as annexes to existing hospitals or for emergency hospitals and assign cadre organizations; (5) determine the number of patients that could be cared for in these facilities; (6) request the supplies that are required, in writing, through existing channels; (7) attempt to obtain "housekeeping equipment" locally if possible; and (8) reserve existing hospital beds for patients with the most serious cases and try to care for the majority of evacuee patients in hospital annexes or in the civil defense emergency hospitals.

Results

Many interesting and important things were revealed when the reports were assembled and broken down on the evaluation sheets that we developed. Of a total potential of somewhat over 5½ million persons, the support areas reported receiving 4,238,000. These were figures developed by the Welfare Service. On the basis of total population, that is, residents plus evacuees, the calculated number of hospitalizations was 26,775, whereas reported patients amounted to 25,731. There is a difference of just about 1,000 between the theoretical total number of patients calculated on a 4.5 per 1,000 basis and the actual number of patients reported.

Further analysis of the hospitalization figures reveals some interesting developments. There were 19,317 beds available for the 25,731 patients, resulting in a deficit of 6,414 beds. Of the 19,317 available beds, only 9,920 were actually used, leaving 9,397 that were not used. At first glance this seems to be a bit incongruous. The explanation is very simple and shows what we considered to be good planning on the part of the reception areas. Instead of putting all of the evacuee patients in the existing hospitals, they activated the civil defense emergency hospitals and also set up emergency hospitals in schools, hotels, and other suitable buildings. This left a reserve of almost 10,000 beds available to be used for casualties if an attack should have occurred. It also would give them an opportunity to use the unfamiliar emergency hospitals for an unknown period of time for the care of patients requiring little medical supervision, prior to the receipt of casualties. This in effect would be a very practical "not so dry run" or, if we could borrow the parlance of the theatrical world, a dress rehearsal.

Analysis of the data concerning the use of the emergency hospitals leads to only one conclusion: we at the upper levels of state-wide planning have not completely put across to those in the reception areas our doctrine for the use of these hospitals. Our concept is to use these hospitals as nuclei around which will be built hospitals with capacities of 500 to 1,000 patients. The reception areas reported that they needed 61 emergency hospitals and that there was a deficit of 44. On the basis of units actually available in the region at that time, including 14 in the then FCDA warehouses, this figure should have been 27 instead of 44. How much of this discrepancy can be accounted for on the basis of consolidation of reports at successive echelons we do not know. This is only one of the many perplexing problems that could occur during actual operations. Based upon paper calculations, the actual number of emergency hospitals that would have been required should have been from 6 to 12, instead of the reported 61, and instead of a deficit there should have been from 22 to 28 hospitals that were not used and were still in reserve for use for casualties. This is a large problem that we must work on.

The use of first-aid stations was also very interesting. Almost universally, the reception areas assigned first-aid stations to mass care and reception centers for the center from which medical care would be given to the evacuees. They committed 212 stations of a total of 353 in the region. Theoretically there should be 141 stations remaining, but actually this was not the case. Many of the first-aid stations were in the evacuated areas; in fact, there were ony 201 stations stored in the support areas, so there was an actual deficit of 11 stations in the support areas. Another lesson for us was that the first-aid stations cannot be assigned for any other than their intended use and especially cannot be used as superdispensaries in the support areas. We cannot simply tell the people in the support areas not to use them for that purpose. We have to develop something else for this purpose, and we are working on it.

The reported use of blood was another area that was perplexing and apparently not realistic. For the total number of 25,731 patients, there were requested 53,463 blood procurement sets, which logically should translate into an equal number of units of blood required. This is an average of slightly over two units of blood per patient. In an effort to arrive at actual use of blood for everyday purposes in this locality, figures were obtained from the Los Angeles Red Cross Blood Center. In the area serviced by that center, 179,095 units were used in the last year. In this area there are 35,580 beds. With an occupancy factor of 80%, unless my mathematical methods are erroneous, the average use of blood would be 0.175 units per patient for a 10-day period. If these figures are correct, the theoretical requirement should have been 4,500 units. The only logical explanation must be that, in most instances, the reporting support areas were using the blood requirement figures for casualties as the basis for their requests.

Personnel shortages were reported for all categories except veterinarians. In some of the reports it was extremely difficult to reconcile the figures, which is another example of the difficulties that we must expect during actual major disaster operations. There was not one category in which it was possible to subtract the number available from the number required and have the figure equal the reported deficit. Regardless of the cause of these discrepancies—mathematical or typographical errors, faulty message transmission, or some other factor—the fact remains that we must expect erroneous situation reports and take this into account when distributing our available resources. The one fact that stands out is that even in this strategic evacuation, without casualties, there were shortages of significant numbers. Some of these were physicians, about 1,000; nurses, 2,300; pharmacists, 110; nurses aids, 5,000; and laboratory technicians, 280. How much of these deficits could be made up from the evacuees is a matter of conjecture, but we feel that it is safe to assume that after several days there would actually be surpluses of physicians and nurses and probably of pharmacists as well. It is very doubtful if there would be enough nurses aids among the evacuees to meet the requirements. The data concerning first-aid workers was so contradictory and apparently unrealistic that we had to eliminate them from evaluation.

Even with all facilities intact, some areas reported shortages of water and resorted to rationing. This also forced limitation of the use of waterborne sewer systems in some areas, requiring latrines or other means of dry sewage disposal. In still other areas the systems were overloaded, so that at peak flows it was necessary to divert into impounding basins.

Some of the counties felt that it was desirable to do mass immunizations against typhoid-paratyphoid but realistically recognized that it would be difficult, if not impossible, to obtain the required vaccine.

It was gratifying to know that, without exception, all reporting levels agreed that this was the most beneficial and practical exercise that they had participated in. Much information was obtained, many lessons were learned, and defects were found. It was encouraging to learn that without exception any conflicts in the desired use of buildings could be resolved locally, so that arbitration at a higher level was not necessary.

Summary and Conclusions

In a California disaster exercise, the hospitalization problem was solved by activation of emergency facilities, thereby reserving approximately half of the available beds for potential casualties as well as affording the opportunity of familiarization with emergency hospital units before casualties would be received. We have not succeeded in conveying our doctrine for the use of emergency hospitals to the support areas. There were a number of unexplainable discrepancies in reports, making some of them valueless or open to question. Although this is an operational condition that is certain to develop, we must renew our efforts to minimize such occurrences. It is a tactical error to commit first-aid stations for use as dispensary-infirmaries. It is imperative that an acceptable unit be developed for this purpose. The use of blood was entirely unrealistic. As anticipated, personnel shortages were almost universal, although in the most important categories it is believed that the shortages could be overcome in a reasonable period of time. Even with intact supply systems, water shortages developed. In some parts of the United States there would be no problem with this, whereas in others it could be very serious. Sanitation facilities were overburdened or inadequate, requiring reversion to primitive methods. Mass immunization was shown to be practically impossible.

It was felt to be worthwhile to share with you our experiences in this different but very practical form of test exercise, and we suggest that exercises of this type could well be conducted in most of the target areas.

THE STORY OF "OPERATION PREP PITT"

PITTSBURGH'S FIRST DISASTER DRILL WITH SIMULATED CASUALTIES

Francis C. Jackson, M.D., Pittsburgh

The promotion of disaster planning in a community is, at best, difficult and, for certain, unpopular. The disinterest of the public has been attributed to a sense of hopelessness with regard to protection from atomic warfare, to irresponsible planning and inconsistent leadership by government agencies, and to a sense of apathy with respect to the infrequent occurrence of natural disasters.[1] Catastrophe never seems to be imminent.

However, since the medical profession assumes a vital and responsible role in times of disaster, it behooves its membership to persist in preparing itself and in cooperating with other community agencies concerned with health and welfare prior to such catastrophic events.

Although confusion has existed with regard to the functions of physicians within the structure of the civil defense program,[2] there has been no question relative to their traditional responsibilities in their respective hospitals during a disaster in the community. In general, the profession has, heretofore, found itself in an advisory capacity to this agency with little impact on governmental attitude.[1]

The fact that the civil defense program overlooked recurring natural disasters prompted the American Hospital Association to change the title and scope of its Committee on Civil Defense to, simply, that of the Committee on Disaster Planning.[3] The admonition by some authorities[1] to "play down the bomb" implies "play up the hurricane" as a more practical approach to the problem. Dedicated planning by general hospitals to cope with mass casualties to be expected from natural disasters, in theory, would provide a basic organization for national emergencies of a much larger caliber. Certainly, the motivation in organizing for the former is characteristically attended with greater enthusiasm. In any event, the hospital remains as one of the traditional centers for survival by a community.

Recently, the county medical society has been proposed as the "coordinator" of health services for all disaster agencies.[4] The feasibility of this ambitious concept was successfully demonstrated in "Operation Test Star" supervised by the Alameda-Contra Costa (Calif.) County Medical Society in June, 1958. Actually, this vast exercise was the effective coordination of a number of individual hospital disaster plans throughout the counties involved in the exercise.

Problems and Plans of the Allegheny County Medical Society

In September, 1950, a special Advisory Committee to the Office of Civil Defense in Pittsburgh was created by the Allegheny County (Pa.) Medical Society. Four years later this committee was still attempting to develop functional relations with civil defense groups.[5] Finally, in accord with the general trend noted above, the name of the committee was changed in 1957 to, simply, Disaster Committee. With this broadened frame of reference, the new group was able to engage itself in the full range of disaster preparedness.

In November, 1957, a subcommittee on hospital disaster planning was appointed. The Hospital Council of Western Pennsylvania, with a membership of 70 hospitals, generously offered its support, an association which assured a continuing liaison with the hospital administrators. The end result was the creation of a Joint Committee for Hospital Disaster Planning with a co-chairman from each organization.

The new committee provided itself with 10 major goals: (1) to promote a disaster plan for each member hospital of the council; (2) to guide and assist, when requested, the disaster committee of each hospital in the preparation of such plans; (3) to encourage "dry runs," rehearsals, and "field trials" of such plans; (4) to assist in the coordination of these plans with those of other disaster agencies in the community; (5) to conduct periodic surveys for the assessment of the disaster preparedness of hospitals; (6) to establish a library of disaster information; (7) to prepare and distribute a cumulative bibliography devoted to the management of disasters and allied information; (8) to provide a regular newsletter for hospital disaster committees; (9) to conduct annual "seminars" devoted to all aspects of disaster management; and (10) to sponsor an annual disaster drill at one of the hospitals in the area.

The first survey was conducted in January, 1958, and produced a response from 43 of the 70 member hospitals. Thirty-two administrators indicated that their plans were completed. However, only 14 had ever tested these plans. Therefore, it seemed opportune for the joint committee to sponsor a casualty management exercise at an early date.

First Annual Mass Casualty Drill

To coincide with "Operation Alert, 1958," May 6 was selected as the date for the first demonstration drill sponsored by the joint committee. The name "Operation Prep Pitt" was selected as the title for

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Chairman, Hospital Disaster Planning Committee, the Allegheny County (Pa.) Medical Society.

the event. A VA hospital was chosen as the site for the exercise for several reasons. It was adjacent to the medical school; it did not have a complete and detailed disaster plan; the majority of the members of its medical staff were resident physicians; the VA was prepared and willing to coordinate its disaster organizing with local disaster agencies; and, finally, the National Damage Assessment Agency had indicated that VA hospitals would probably serve as casualty centers in the time of a national calamity.[6]

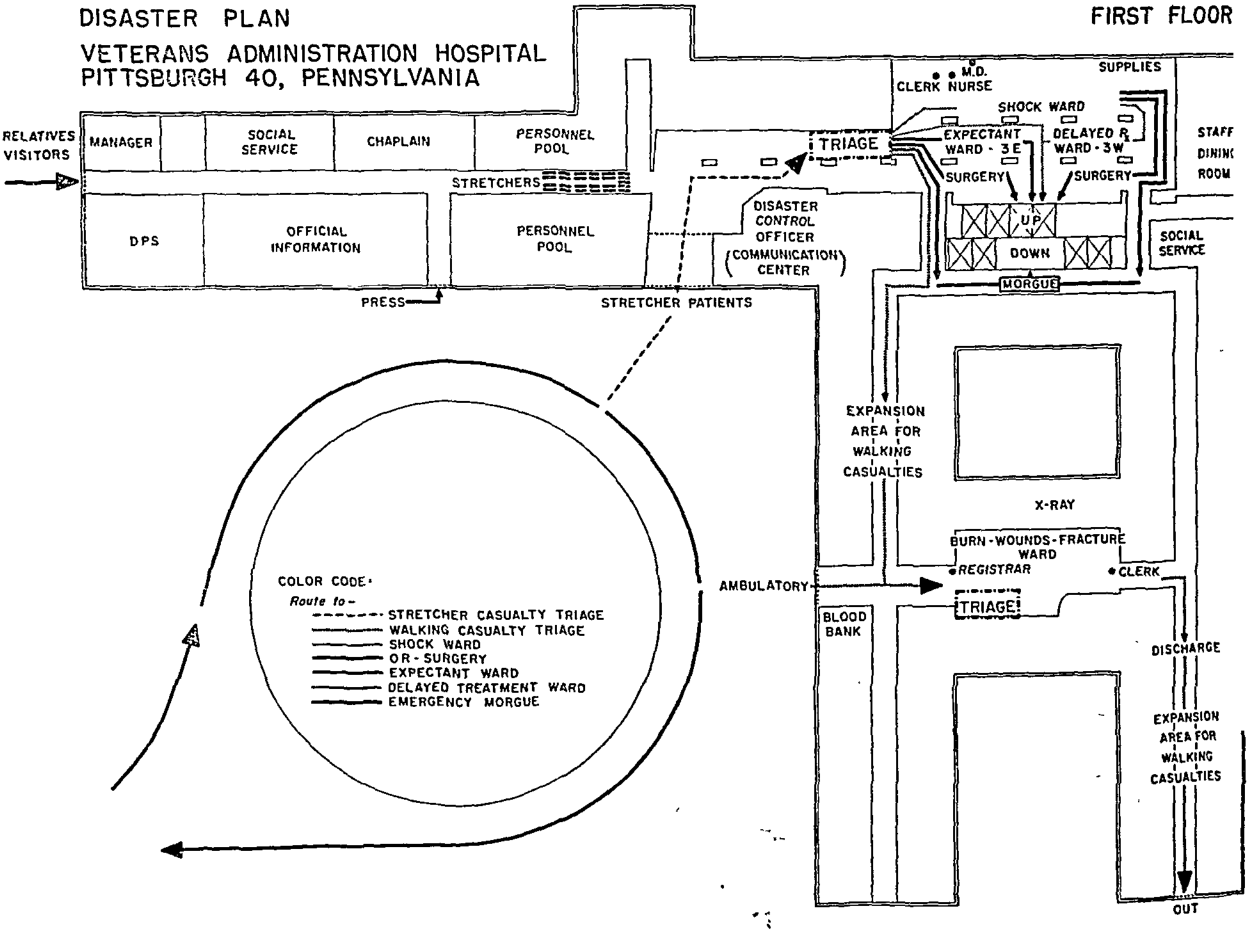

Fig. 1.—Routing organization for stretcher and ambulant casualties for first floor. Principle sections of care are adjacent to arrow routes. Color codes were assigned to each stretcher casualty, indicating his destination as follows: green, shock ward; red, operating room; blue, expectant ward; yellow, delayed treatment ward; black, emergency morgue.

"Operation Prep Pitt" was to provide a "disaster showcase" not only to encourage preparedness in western Pennsylvania but to test three selected aspects of casualty management by a general hospital: (1) the mobilization and expansion of medical facilities, (2) the "military" system of mass casualty care, and (3) the effectiveness of the civil defense emergency medical tags, records, and information cards.

The second aspect was considered to be the most important feature of the exercise. The application of military principles of medical care, so highly successful in wartime,[7] has long been overlooked or even depreciated by civilian physicians.[8] However, it must certainly be appreciated that there can be no differentiation, now, between "civilian" and "military" care in the handling of mass casualties.[9] The number and character of injuries to be anticipated in the next national emergency will, unfortunately, be similar. Therefore, the recommendation that an effective sorting system which provides only lifesaving care for casualties with minimal injuries (up to 60% of estimated survivors) should be established in civilian hospitals has considerable merit.[10] It is also well to note that, whenever civilian physicians with military experience in mass casualty care have participated in a large civilian disaster and have applied these principles, the results have been eminently satisfactory.[11] For these reasons the committee incorporated the "field" type of casualty flow organization into its first annual disaster exercise.

The casualty load selected was only 50, a number which would severely tax the facilities of almost every hospital in the area. The dean of the University of Pittsburgh School of Medicine and the MEND coordinator arranged for the freshman class to volunteer their services as "casualties" and "anxious relatives." Medical students are "reliable" casualties and proved "ham actors." [12]

Through the office of the commanding officer, Army Medical Service School, Brooke Army Medical Center, Fort Sam Houston, Texas, a staff sergeant was detailed to supervise the creation of simulated "injuries" by other volunteer students. The use of "make-up" was to prove particularly effective in the orientation of triage officers and in encouraging enthusiastic participation of the ancillary hospital personnel.

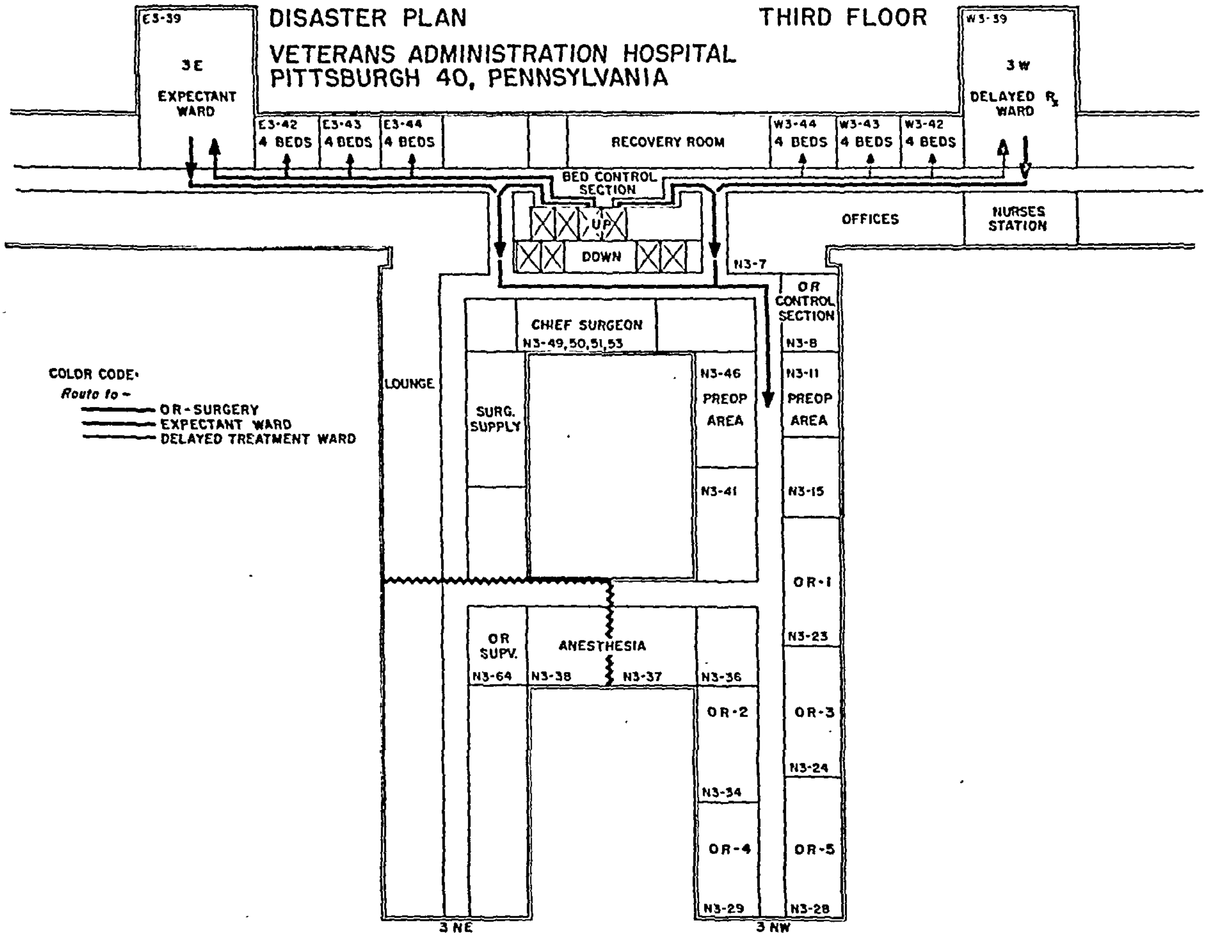

Fig. 2.—Casualty flow chart for third floor. East wing received more seriously injured, while west wing provided temporary care for those whose definitive treatment was delayed. Note locations of bed and operating room control.

A directing or planning commitee was created from respresentatives of each of the 16 major hospital divisions. A tentative casualty flow chart was designed on a portable blackboard, and, at two weekly meetings in the month preceeding the drill, the senior officers in charge of stations along this route (fig. 1 and 2) made changes or improvements. The assignments of personnel, equipment, and supplies were left to the decisions of the section chief and their staffs. Ultimately, 218 employees received drill assignments. However, it should be emphasized that only broad, basic instructions were given so that, as a group, the participants were relatively unprepared for many of the problems that ultimately transpired. The final disaster plan for the hospital was to be written from the experiences of a "created" natural disaster—in this instance a jet-plane crash on the University Field House two blocks away.

Casualty Flow Plan

Although there are many and, occasionally, insoluble problems in the construction of an organization for mass casualty care, the use of a unidirectional route of flow for the injured within the hospital area appears to be the key to its success or failure. The plan evolved for "Operation Prep Pitt" (fig. 1 and 2) took into account the architectural features of the VA hospital: principally, two large spacious foyers which provided direct access to the entrances, elevators, and halls (i. e., routes for the distributing or discharge of casualties); the location of the regular center of communications; and the location of the primary treatment center, the operating room.

Traffic control at the hospital entrance or "offloading" area was simplified by directing ambulances counterclockwise in order to prevent congestion in the main drive, a situation which has completely inactivated hospitals in natural disasters.[13] By arbitrary provision of labeling of entering persons as "stretcher casualties" and "walking casualties," an automatic sorting of the injured was provided at the hospital door. Since a connecting roof covered the sidewalk between these two entrances, immediate redirection, if necessary, could be accomplished without the confusion of transport within the hospital.

Twenty service points, or sections, along the route within the hospital were devised to give continuing support to the injured. Ten of these were regular or fixed hospital divisions (such as pharmacy and laboratory), and shift of location or altering of duties was not required. The 12 considered most important are listed in the table, with their assigned duties, capacity, and personnel. The remaining sections were blood bank (donor section), laboratory and x-ray departments, central sterile supply, social service and chaplain sections, security force, and information center. Fifty-six members of the hospital staff were located in these particular areas.

Ambulant Casualty Care.—It was planned that one-half of the casualties provided for the exercise would have sufficiently minor injuries to enable them to walk into the hospital. This section was to be well removed from the entrance through which the stretcher casualties were to be received (fig. 1). It was necessary to "set-up" these facilities from preloaded carts, since an outpatient department is not an integral part of VA hospitals. Those with burns, closed fractures, and soft-tissue wounds were to receive prompt, basic treatment so that immediate discharge of the casualties reporting could be effective. Tetanus toxoid or antitoxin was to be administered if time permitted. Otherwise the follow-up instructions issued to the dischargees from this section noted this omission. The social service department operating in this area was to provide assistance and clothing and arrange for transportation. The logging of the ambulant casualties was to be expedited by collecting their emergency medical tags and completing the index and information cards.

Hospital Organization for "Operation Prep Pitt"—Twelve Key Sections of Casualty Flow

Section or Officer*	Duties or Activities	Capacity	Personnel
1. Disaster control	Supervise and organize evacuation and expansion; maintain communication with disaster site and other community disaster agencies; provide assistance and supplies on demand from hospital sections	...	3 Physicians, 3 messengers
2. Triage officer	Sort and direct stretcher casualties to sections along casualty flow route; maintain log of admissions	...	1 Physician, 1 clerk
3. Shock ward	Treat shock, provide airways, splint fractures, relieve pain; retriage as soon as possible	12 Mobile litters	3 Physicians, 3 nurses, 3 nurses aides, 3 technicians, 2 clerks
4. Delayed treatment ward	Cover wounds, apply splints, treat shock, and prepare casualties for later care; arrange priority of transfer to operating room	40 Beds (28 evacuated)	3 Physicians, 3 nurses, 3 nurses aides, 2 clerks
5. Expectant ward	Provide general supportive care; prepare to retriage, if necessary	40 Beds (28 evacuated)	Same as delayed treatment ward
6 Bed control	Maintain log of ward admissions; notify disaster control officer of need for expansion		1 Clerk
7. Operating room control	Prepare casualties for anesthesia; select qualified operating team for each casualty; provide consultation and relief to operating teams	10 Casualties	3 Physicians, 2 nurses, 2 nurses aides, 1 clerk
8. Operating room (surgical teams)	Lifesaving measures only; stop hemorrhage; débride wounds and pack open; close sucking chest wounds and perforations of bowel; cover tendons, arteries, and bone and revise amputations	5-10 Casualties	16 Physicians (4 in relief), 2 dentists, 9 nurses (2 in relief)
9. Emergency morgue	Identification, finger printing, collection of personal effects	20-30 Dead	2 Clerks, 2 technicians
10. Ambulant casualty section	Emergency care of wounds, burns, and simple fractures; administer tetanus toxoid or antitoxin; issue follow-up instructions	4 Treatment tables, 1 plaster table	3 Physicians, 2 nurses, 2 nurses aides, 3 clerks
11. Communications	Notification of key personnel; keep disaster control officer informed of incoming reports		3 Operators, 2 "walkie talkie" operators, 3 messengers
12. Personnel pool	Provide stretcher, chauffeurs, messengers on request		50 Volunteer employees

* Locations given in figures 1 and 2.

Stretcher Casualty Care.—The more seriously injured were to be off-loaded (fig. 3) from the ambulances by volunteer personnel (maintenance employees) and then placed on mobile litters manned by chauffeurs from the personnel pool (fig. 1). Twenty-five of these litters were to be stored in an adjacent corridor during the alert. In theory, emergency care, including the treatment of shock or surgery, could be performed on this unit without transfer of the injured. Immediate sorting was to be completed by a triage officer in the wide admission foyer. Assisted by a clerk, he was to assign each casualty a color designation (an adhesive strip placed on the forehead or medical tag) in order that the chauffeur could follow a color route (also labeled) to one of five centers, i. e., shock ward, expectant ward, delayed treatment ward, operating room, or emergency morgue. With the exception of the shock ward, the remaining treatment sections were on the third floor (fig. 2). The elevators located nearest to the triage officer and the shock ward were converted to an "up" system and those in the rear to a "down" system. There was to be flexibility in the operation of these elevators manned by the security section. Three of the stretcher casualty sections listed in the table might be elaborated on.

Shock Ward: The shock ward was immediately available in the triage area (fig. 1) but sufficiently well separted so as not to interfere with other traffic originating from it. There was to be sufficient room for 12 or more of the mobile litters. Since the majority of persons injured in a natural disaster are admitted in a state of shock,[14] it was deemed important that this unit be immediately available and ready to treat shock as well as all injuries contributing to shock. Airways were to be reestablished, malaligned extremities splinted, wounds covered, and pain relieved. Retriage would require the assignment of another color designation for the casualty.

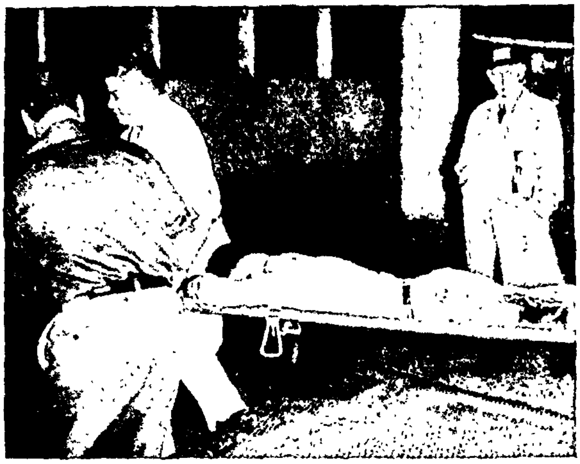

Fig. 3.—Umpire supervising off-loading from ambulances by untrained volunteer personnel.

Bed Control Officer: The need for further expansion of ward facilities during the height of the drill might not be immediately reported by busy personnel to the disaster control officer. Therefore, a clerk, designated as a bed control officer, was to be stationed opposite the "up elevator" system on the receiving wards to log the admissions and maintain contact with the disaster control officer (fig. 2).

Operating Room Control Officer: The operating room control officer was considered almost equal in importance to that of the triage officer (fig. 4). This officer was to be an experienced surgeon who was to reassess casualties, retreat shock, supervise the administration of preanesthetic medicaments, and assign the casualty to one of the skeletonized operating teams in accord with their talents. He was also to provide consultations and relief for these teams and to maintain contact with all areas where casualties were awaiting further care.

Performance of the Exercise

May 6 proved to be a wet, windy, unseasonable day so that the traffic signs on the exterior of the hospital promptly blew down. Ten minutes after the hospital received the alert at 8:15 a. m., its ambulances were dispatched. Evacuation of 60 patients on wards 3-E (expectant) and 3-W (delayed treatment) was completed at 8:46 a. m. on directive from the disaster control officer. The first casualties were arriving by 9:02 a. m., at which time all sections were prepared to function. The wounds of the medical student casualties immediately created the satisfactory illusion of reality.

The ambulant casualty section was quickly overwhelmed by the simultaneous arrival of almost all the injured able to walk. The logging and identification of admissions fell so far behind that "anxious relatives" created mild consternation in the social service and information sections and then eluded the security guards to arrive at the bedsides of the injured. Although regular communications function well, the number of messengers was inadequate. However, the "walkie-talkie" units functioned exceedingly well inside the building. The absence of a place for noting the religious faith on the emergency medical tags was criticized, as was the fact that registry numbers were not assigned to those admitted. The most satisfactory demonstration was the performance of personnel in the shock ward and the operating room, where few if any errors in casualty care were observed. Within 90 minutes of the first arrival, all casualties had been evaluated and 14 procedures carried out in the operating rooms.

Rating of the Exercise.—A critical evaluation of "Operation Prep Pitt" was provided by a team of five qualified umpires. The chairman was Harry E. Feather, M.D., associate professor of surgery at the medical school and former chief of surgery of the 27th General Hospital of the U. S. Army during World War II. The exercise was rated on a 24-point questionnaire which required opinions as to the location, organization, and effectiveness of the sections along the casualty flow route.

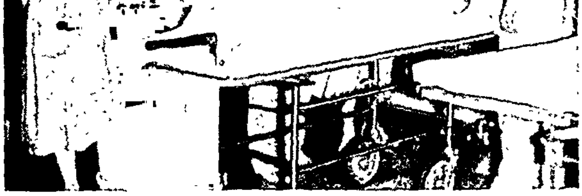

Fig. 4.—Even in operating room control section, casualty remains on original litter. Movement is thereby kept to minimum.

The umpires considered the best feature to be the handling of the litter casualties, particularly in the shock ward and operating rooms. The delay in the identification of the casualties and the dissemination of information were rated as the poorest features. The civil defense index and information cards were considered ineffectual for their designed purpose.

The handling of the injured at the off-loading area and on admission to the ambulant casualty section was also rated as poor for reasons previously noted. The color routing system was approved, but larger signs and diagrams were suggested.

In conclusion, the drill was rated excellent in 11 areas, good in 5, fair in 2, and poor in 5. A strong recommendation was made that the exercise be perpetuated on an annual basis.

Since "Operation Prep Pitt" was held, four other hospitals in the Pittsburgh area have held drills with simulated casualties. Others have indicated similar intentions.

Summary

"Operation Prep Pitt" was the first annual disaster drill to be sponsored by the Allegheny County (Pa.) Medical Society and the Hospital Council of Western Pennsylvania. It was attended by 147 official representatives of these organizations.

The "military" management of mass casualties by civilian hospitals preparing for disasters could be considered preeminent training for casualty care in time of national disaster.

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GENERAL PUBLIC HEALTH PROBLEMS IN CIVIL DEFENSE

Lieut. Col. Ingalls H. Simmons (MC), U. S. Army

Abraham Lincoln stated the major problem of disaster survival succinctly when he said, "You can't escape the responsibility of tomorrow by evading it today." Although no one at present has all the answers to the problems of survival in mass disaster, it is most important that we become acquainted with the answers we do have and begin thinking of possible solutions to problems which we know may arise in our particular situations.

Major Gen. James P. Cooney, deputy surgeon general, has classified people involved in disaster into five major types: the overly optimistic, the very religious, the fatalistic, the ultraneurotic, and the sensible. The optimist is convinced that whatever is going to happen to him is all for the best. The very religious type dismisses the problem, too, by declaring, "Let God's will be done." The fatalist believes he is safe until his number comes up, and there is not much he can do about it anyway. The ultraneurotic person may even go out and commit suicide to keep from being harmed by the atomic bomb. The sensible type is the only one who takes a positive approach to the problem: he attempts to plan ahead and to learn everything possible to protect himself and others, should disaster occur. The attitude of the sensible type is the one we should all try to have.

Our thinking in terms of disaster situations may be stimulated when we consider, for example, that at Hiroshima approximately 70,000 persons were injured and about the same number killed when the atomic bomb fell on that city. At Nagasaki about

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40,000 were injured and very close to the same number killed. Foregoing a bit of our culture and comforts and getting down to basic essentials, we realize that the first necessities after a disaster will be water, food, and shelter.

Initial Survival Period

In every home, in every eating establishment, and in many office buildings there are excellent sources of emergency water supply—sources which in the confusion of disaster we are apt to forget, even though they are close at hand. Water in bottles in the refrigerator and from melted ice cubes is perfectly safe and protected. Water-packed canned fruits and vegetables will also provide a good source of water. The home water heater, which usually contains at least 25 gallons of water, can be drained by opening a tap at the bottom. A minimum of 7 gallons of water per person per week is the recommended amount.

On the shelves in most homes can be found a fairly adequate supply of emergency foods, such as canned fruit, fruit juices, vegetables, meats, soups, canned or powdered milk, baby food, raisins, packaged cereals, and dried food, which are all excellent, safe food. Each family should keep on their shelves an adequate supply of foods of this type and should rotate them frequently, as many may deteriorate.

The requirement for shelter, the next consideration, will vary with geographical and seasonal situations. There is a great difference between what is needed for adequate shelter in New York City or Chicago in the middle of winter and the South in summer. Shelter includes not only buildings but some sort of body covering, such as clothes, blankets, and sheets. If a disaster occurs in the middle of the night, many people may not be adequately clothed. Consideration must be given to the age and physical condition of the people. Secondary hazards in shelters can occur from escaping gas, from leaks from gasoline storage tanks, from electricity, from man-made fires or collapse of buildings.

Later Survival

After the initial survival period, added to the problems of thirst, hunger, and shelter will be others: insect and rodent control, stray animal control, waste disposal, proper handling of bodies, immunization, personal hygiene, dissemination of information, pharmaceutical and laboratory supplies, obstetrics, and care of premature infants, little children, and the aged. Survival during the initial stages after a disaster is predicated largely on the initiative and preplanning of the individual; later, continued survival depends on the prior planning of the community.

Another imposing problem—the obstetrics problem—is often overlooked in planning. During the bombing of Hiroshima, 27% of all pregnant women had abortions, miscarriages, or normal deliveries. Survival of the United States is dependent on the survival of children and of women of child-bearing age. Any plan must consider care of postnatal and premature infants, as well as normal infants. Other special nursing problems will include care of aged persons and children whose parents are lost or dead.

The proper handling of bodies is a major problem which people do not like to face. What will be done with from 30,000 to 100,000 bodies? Disposing of them in individual graves would be an impossibility. Stacking and cremating them would be unsatisfactory because 40% of the material would remain to be disposed of in another way. The best method appears to be the large, mass grave. The bodies with whatever identification is available should be placed in it and buried. Later on, when the situation is better, they might be exhumed, identified if possible, and given separate burial.

Still another problem is the dissemination of information. Everyone should have a small battery radio with the dial marked with small diamonds pointing to the Conelrad stations. These stations may well be the sole source of information concerning high points of radiation and location of supplementary water, food, shelter, and medical aid.

Individual Measures for Survival

Survival after a disaster comes in steps. If you survive the original event, it is only by preknowledge and preplanning that you can continue to survive until another event, natural or man-made, takes your life. Planning for community survival must necessarily depend upon the survival of individuals. To survive as an individual, you should take the following steps: When you receive warning, close all doors and windows. If possible, back them up with blankets, bedding, bureaus, or something else to prevent the scattering of glass. If you are outside, seek cover in a ditch or in any place that throws a shadow on you; that way, you will get some protection, at least. If you are in a building, seek cover under a bed or any substantial object. At home, if you have a chance, hide under the cellar stairs, or in the corner of the cellar, where you will have at least 3 ft. of dirt between you and the bomb. This is the magic number—at least 3 ft. Wherever you are, always drop flat on your stomach. If you are out walking on the street when a bomb goes off, fall flat, face down, immediately. This is going to be a big American problem, because we are just too curious. Curiosity pays dividends in some ways, but at the time of a thermonuclear bomb it certainly will not pay you to look around to see what is happening. Keep your face down, and count off at least 20 seconds. Do not rush outside; you may rush out just at the wrong moment. You are much safer to stay where you are if you possibly can. This should be especially stressed: know your signals and follow instructions. Remain calm, and don't run wildly about—this may cost injury or death to you or your families.

In disaster situations never take chances with food and water. Just the simple action of turning a can or a box upside down and opening the end that sat on the shelf, the table, or the floor may save your life. Remember that radioactive fall-out material is just like dust. It is as if you took the sweepings in your vacuum cleaner, shook it in front of a fan, and let it blow all over your home. The main problem is to keep fall-out from getting into your stomach, where it can really do damage. Get official information over your Conelrad stations on your battery radio and follow it carefully. Above all, plan and prepare intelligently ahead of time for disaster, so that when it strikes you and others may survive.

Apathy, stupidity, and procrastination can be the cause of more casualties than the initial disaster. To preserve our birthright of life, liberty, and the pursuit of happiness, we must not trust solely in groups, governments, or God but rather plan and prepare intelligently.

AMERICAN MEDICAL ASSOCIATION SPECIAL STUDY PROJECT REPORT

Earle Standlee, M.D., Chicago

Prior to the successful detonation of the hydrogen (fission fusion) bomb in November, 1952, and of the uranium (fission fusion fission) bomb in February and March, 1954, medical aspects of civil defense planning had been concerned primarily with mass casualty care, little or no thought having been given to the care and treatment of noncasualties. Civil defense had been considered more or less in the light of scattered atomic disasters with recuperative responsibilities within the states and their local political subdivisions. This was the apparent concept of the 81st Congress, as stated in Public Law 920 (known as the Federal Civil Defense Act of 1950).

With the advent of the larger weapons and the knowledge of their vastly increased destructive capabilities, civil defense began to take on a newer meaning: national survival with the capability of the surviving population to arise from the ashes of mass destruction and piece together the remaining segments of national economy to support the armed forces in waging war to a successful conclusion. Likewise, the medical problem began to assume correspondingly larger proportions, in that under this concept medical care must now encompass not only the treatment and care of mass casualties but noncasualties as well. In addition, the medical problem would be further compounded by the tremendous loss of professional and nonprofessional medical personnel, as well as a large percentage of existing medical facilities and large segments of the medical manufacturing industry. Medical planners in the federal government (Federal Civil Defense Administration) thus became faced with professional facets which they felt only the medical profession itself could resolve. Included among these was the determination to what degree medical allied personnel, such as nurses, dentists, and veterinarians, could participate in medical care techniques ordinarily reserved for physicians and what training they should have in peacetime to prepare for such participation following mass attack. It was with this in mind that the FCDA sought and obtained a research contract with the American Medical Association to develop criteria needed as a basis of a national emergency medical care plan for the treatment and care of the surviving population in the event of thermonuclear warfare involving the United States.

In the Scope of the Contract, the A. M. A. is called upon to study, develop, and recommend the planning, training, and operational organization needed as the basis for a national emergency medical care plan. It furthermore calls for the A. M. A. to furnish advice and recommendations for an organizational plan which will result in the optimum of medical care to the United States in the event of enemy attack, study and develop recommendations for the utilization of professional and nonprofessional personnel of the medical and related professions in a postattack period to carry out the medical care plan, outline the basic role and emergency medical responsibilities of the medical profession in the immediate preattack and postattack periods, outline those functions and responsibilities of the medical profession that may be properly delegated and performed by paramedical personnel under the general direction of the medi-

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Director, Commission on a National Emergency Medical Care Plan, American Medical Association.

cal profession, furnish advice and recommendations as to the training and education that is needed by all health personnel, professional and nonprofessional, so that they may be prepared for operational capability in the event of enemy attack, and furnish advice and recommendations as to the postattack sorting of casualties.

Activation of the Project

For carrying out its responsibilities under the contract, the A. M. A. created the Commission on a National Emergency Medical Care Plan and vested it with the authority and responsibility for planning, initiating, establishing, and directing the study project.

The Commission viewed civil defense not in the more common and limited concept of being "concerned mainly with rescue operations and services to stricken populations" but rather in the broader concept of its being a dynamic aspect of national defense with importance second only, if not equal, to that of military defense and concerned "with the whole complex of nonmilitary activities necessary to prepare and mobilize the nation's economy against possible war, to survive and emerge from the ashes of attack, to maintain the continuity of government and essential production, and to proceed toward partial recovery and then toward full resumption of peacetime pursuits." The latter concept was that which had been adopted by the Congressional Subcommittee on Military Operations in its studies of "Civil Defense for National Survival."

Major Gen. Otto L. Nelson, who headed the East River Study Project in 1951 and the review of that study in 1955, in a statement to the Subcommittee on Military Operations on March 4, 1956, described briefly the various views on civil defense that seem to have some measure of acceptance. I would like to quote from his statement in indicating these views:

> First of all, there are those who believe that nothing should be done and no money should be spent at all on nonmilitary defense. This view holds that the United States should spend its money and expend its resources on a strictly military defense program in the belief that in this way we get the most for our money and that, as a minimum, we need to spend all that economy can afford on our military fighting forces. In effect, our people, cities and industries have to be considered as expendable because it either costs too much to defend them or, no matter how much is spent, the defense is still ineffective. This view holds that a calculated risk must be taken with respect to our cities, industries and people and that our over-all defense is best served by spending all available resources on strictly military defense.
>
> A second view is quite close to the first, except that it supports a minimum nonmilitary defense program that is admittedly inadequate and ineffective. I suppose that essentially this is a sophisticated attitude which would lead the people of the country to believe that some effective steps were being taken for their protection in an atomic age, although actually the program is so ineffective as to be a total waste of funds involved. Perhaps an extreme way of putting it is to say that, under the concept, one considers the nonmilitary defense task to be so difficult, complex, and expensive that there is no practical or effective solution. However, this is not to be admitted publicly but instead an ineffective, phantom program is set up with appropriate individuals and agencies to serve as scapegoats if such are needed at a later time. In a sense, one might say that this is a "cover plan." Such has been used in military operations in an effort to delude the enemy that military activities were going on in an area with a view toward later military operations which, of course, were not contemplated. In the field of nonmilitary defense, I doubt that such indications of a nonmilitary defense cover plan with ineffective activity would delude an enemy, but it might lull the general public of the United States into a false sense of safety in this atomic age. I suppose the justification for such an attitude is the feeling that for political reasons something must be done, so you make a gesture in the absence of any effective program or the knowledge of how to undertake one.
>
> A third view is that nonmilitary defense ought to be a vital and continuing part of an over-all and balanced total defense program. This view recognizes that our active military defense forces should have first claim on the defense funds that are available. Certainly, a strong balanced armed force of land, sea and air elements is needed, capable of fighting an atomic war or available to block the Soviets' use of power politics through satellite countries where resource to atomic weapons might be avoided. In addition, there is needed the continuing maintenance of the military might needed to strike a crushing retaliatory atomic blow against an aggressor.

In its studies the Commission followed the concept outlined in the third view. In laying the groundwork for its study, the Commission elected to obtain material from the following sources: (1) a hypothetical 20-megaton ground burst thermonuclear attack upon a selected geographical area, (2) planning data developed by the several states in their critical target areas, (3) pertinent literature, including governmental and nongovernmental publications, and (4) conferences and communications with appropriate agencies and individuals.

In making its selection of a geographical area for study, the Commission gave consideration to five selected areas before making final decision on the Minneapolis-St. Paul complex. The reasons for selecting this area were as follows. It is included in the FCDA list of critical target areas. Both cities can be destroyed with a single 20-megaton ground burst attack. The area has available space relationships for radius utilization in all directions. A river (Mississippi) runs through the center of the target area. The overflow into Wisconsin brings in political factors. The surrounding area abounds in food and water. Civil defense planning, including medical, was reputed to be well advanced. Good working relationships were reputed to exist between persons and organizations concerned. Top level leadership exists and has a high degree of motivation. Good health personnel and facility data were reputed to have been developed. The Mayo Clinic and affiliated facilities, with 800 physicians and capacity for expansion to 9,200 beds, provides an asset outside the target area. The state of Minnesota reputedly has an effective civil defense legislative act which provides for strict discipline in the event of a major emergency.

Approach to Study

The Commission then approached the study on a four-phase basis as follows:

Phase 1.—Fact-finding and data gathering were attained by observation of planning activities, demonstrations, staff exercises (Operation Alert 1958) in Minnesota, and mass casualty courses given by the Army; by review of planning data in Minnesota and the various (36) other states; by conferences with planning personnel in Minnesota; by conferences and meetings with representatives of the Minnesota Medical Association and Hennepin County (Minn.) Medical Society; and by review of published literature. The latter includes hearings before the subcommittee (Holifield) of the Committee on Government Operations, House of Representatives, 84th Congress, 2nd Session, 1956; extracts of hearings, prepared statements, and Report of the Medical Service Task Force of the Commission on Organization of the Executive Branch of the Government, 1954 (Hoover commission); reports of civil defense conferences; articles on medical aspects of civil defense published from time to time in THE JOURNAL, *Minnesota Medicine, California Medicine,* and *Canadian Medical Association Journal;* and pamphlets, bulletins, and other literature published and disseminated by the Office of Civil and Defense Mobilization.

Phase 2.—Analysis of data and findings involved examination and classification, evaluation—weighing the important relevance of each, and determination of their relation to each other and to other similar existing data.

Phase 3.—A tentative generalized plan outline was developed.

Phase 4.—Conclusions were developed and recommendations submitted.

Participation of Medical Organizations.—From the beginning; the Commission considered it essential to bring into the research study, on a participating basis, national health and medical organizations which would be directly involved in the medical management and care of the surviving population in the event of an enemy mass attack on the United States. After due consideration, it was decided that such participation would, under the circumstances, best be effected by the establishment of appropriate task forces to assist the Commission in its study project.

This concept was concurred in by representatives of the following national organizations: American College of Surgeons, American Dental Association, American Hospital Association, American Nurses' Association, National League for Nursing, American Public Health Association, and American Veterinary Medical Association.

Task Forces

Three task forces were established to assist the Commission in its studies of the items specifically called for in the contract: Task Force on Organization, Task Force on Personnel Training and Utilization, and Task Force on Emergency Medical Care.

The Terms of Reference of the Task Force on Organization called for two areas of consideration in its studies: (1) that of a national organization with its mission, organizational structure, position in the national plan, and channels of communication with delegation of responsibility and authority and (2) that of a local organization with its various elements of organizational structure, their functions, and operational procedures. The following organizations participated through representation in this task force, under the general direction of the A. M. A. study group: American College of Surgeons, American Public Health Association, American Hospital Association, American Dental Association, American Nurses' Association (also representing the National League for Nursing), and American Veterinary Medical Association.

In its Terms of Reference, the Task Force on Personnel Training and Utilization was called on to recommend the manner in which the various categories and numbers of health personnel surviving a mass attack could best be utilized to cope with the many varied and complex medical problems with which the nation immediately would be faced. It also called for recommendations for the development of policies, means, methods, and programs for the training and education needed to prepare all health and medical personnel, professional and nonprofessional, for occupational capacity in the event of enemy thermonuclear attack. The following organizations participated in the studies of this task force: American College of Surgeons, American Academy of General Practice, American Public Health Association, American Hospital Association, American Dental Association, American Nurses' Association, American Veterinary Medical Association, and American National Red Cross.

Terms of Reference for the Task Force on Emergency Medical Care called for consideration to be given to every possible means and methods of casualty management that would provide optimum care under mass attack circumstances. It was also asked to consider the desirability and practicability of utilizing paramedical personnel to perform under the supervision and direction of physicians certain medical functions, particularly lifesaving functions, ordinarily performed by physicians themselves. Its Terms of Reference pointed up the problem of triage or sorting, and the task force was asked to give consideration to the development of medical methods and means of maintaining the personnel resources of the United States with the maximum strength possible under the circumstances to assure the nation's survival. The following organizations participated in this task force's studies: American College of Surgeons, American Public Health Association, American Hospital Association, American Dental Association, American Nurses' Association, and American Academy of General Practice.

National Civil Defense Studies

In conducting its studies, the Commission has taken advantage of two exhaustive inquiries, one on the subject of civil defense for national survival and the other on medical planning for total war. The first of these two was conducted over a period of a year by the military operations subcommittee of the Committee on Government Operations, 84th Congress, 2nd Session, commonly referred to as the "Holifield subcommittee." The other inquiry was conducted by the Medical Services Task Force of the Commission on Organization of the Executive Branch of the Government, commonly referred to as the "Hoover commission." The report on this study was published in 1954, while that of the Holifield subcommittee was published in 1956. Both studies gave strong emphasis to the need for a shift in civil defense responsibility from the states to the federal government in civil defense planning. The Holifield subcommittee strongly recommended that the federal agency charged with this responsibility be required to formulate a master plan for nationwide civil defense and that such plan be pointed toward the establishment of an integrated, nationwide civil defense system.

The medical task force of the Hoover commission in its summary and conclusions stated that "a complete medical plan is an inescapable requirement for survival in an atomic age. Our nation does not have such a plan at this time [1954] nor is it possible to formulate one without some drastic revisions in national policies and organization. As a nation we are grossly unprepared, medically, for total war. Present attempts at wartime medical planning, in our opinion, are ineffective. Multiple approaches to the medical problems of civil defense, which have been adopted by the various states, have resulted in an uncoordinated and inoperative program. . . . Failure to take forceful and aggressive national action to prepare ourselves medically and otherwise for devastation and destruction of atomic warfare is, in our opinion, an open invitation to disaster."

Organizational Criteria

In developing its criteria, the Commission made the assumption that "a Federal agency charged with the planning for, and capable of directing, the recovery efforts of the United States following a mass attack thereon, and so integrated into the Federal government as to assure coordination between all interested agencies, both prior and subsequent to such an attack, not only is necessary, but is attainable." It furthermore assumed that "the United States was able and willing to spend adequate funds on a well conceived civil defense plan for the nation."

The Commission views the task of preparing a national emergency medical plan which would, in fact, prepare the nation, medically, for total war, as a tremendous undertaking but one that is not unattainable and that should be initiated at the earliest moment. In its conclusions, the Commission considered the following steps necessary to initiate and develop such a program:

First, a medical planning group would be established at federal level, staffed with an adequate number of specialists to permit an accurate estimate of the current situation, a determination of the medical requirements, an evaluation of the potential medical resources within the United States, and the formulation of plans which, when implemented, will provide the maximum care to the greatest number with the means at hand. The planning group should be under the cognizance, if not the direction, of the OCDM.

Second, on formulation and approval of operational and training plans prepared by the initial group, a training organization would be established as a major division of the operational headquarters to be formed at federal level. The training division would be staffed with an adequate number of training specialists, as determined by the planning group, and composed of many of the personnel of the group, whose missions would have now been discharged. This division, under the supervision of the medical director, would be responsible for preparing the detailed training programs, written material and training aids appropriate for instruction of each level, and grouping of citizens in the United States; distributing and supervising the use of such material; furnishing all manner of advice and assistance in execution of the training programs; providing competent training teams to assist in organizing similar teams at state and other levels; and even conducting training for some of the higher echelons within the profession.

Third, concurrently with formation of the training division there would be organized at peacetime strength the final, permanent, operational medical element of the agency charged with the supervision and control of national survival efforts. This group would become the medical directorate, which would correspond to the Office of the Surgeon General of the Army, Navy, Air Force, or Public Health Service. Formation of the final organization at reduced strength is necessary on completion of the planning phase in order that a functional directing headquarters, capable of immediate expansion and efficient operation, would be available should war be thrust on the country prior to completion of the training phase of the three-step program. On attainment of a satisfactory training state, or at any time deemed appropriate, the training division will be reduced in size and reassigned to the nonprofessional division of the director's office as a training section.

In case of war or impending war, the medical directorate would be expanded to required strength, would become fully operational, and would absorb such personnel of the training division or section as may be required under the then existing circumstances. The determination as to where the medical directorate should function in the federal structure in peacetime has not been made. It is believed, however, that the medical directorate should be a major part of an agency whose functions pertain primarily to survival of the nation after an attack.

Planning Group

In the organization of the medical planning group, the director has a deputy, legal adviser, comptroller, and office administrator. The director is responsible for planning and recommending the organizations, missions, functions, and mode of operation of the future medical directorate, or medical headquarters to include the training division. The deputy assists the director in all of the latter's activities. An office administrator is required to handle the administrative matters within the office. A legal adviser is essential in order that the director may avoid the enunciation of policies and the preparation of plans that may run afoul of federal and state laws and statutes. Legal advice will also be required on matters pertinent to proposed legislation and repeal of hampering legislation.

Subordinate to the director are two major groupings: (1) the operations division and (2) the professional division. The operations division chief and his deputy are the master planners. They have a publications editor to assist in such matters as editing, determining format, and selecting pictures, illustrations, types of paper, and binding, and similar printing problems.

Organization Branch.—The organization branch of the operations division would have primary responsibility for determining and designing or redesigning the medical field organizations of all types required to provide casualty and noncasualty care to the surviving population. Such organizations would include first-aid stations, field hospitals, specialty treatment centers, specialty teams, convalescent hospitals, holding units, medical supply depots, and motor, rail, water, and air evacuation units, among others.

Plans Branch.—The plans branch would determine the number of field assemblies of the various types required and the allocation thereof to the states; choose the storage sites for assemblies, supplies, and equipment held in strategic reserve; prescribe the doctrine relative to the employment of field units, fixed installations, and nonmedical personnel; devise plans that will assure the necessary communications and transportation facilities for emergency situations; prepare the plans that will assure that the general public is adequately informed of the problems involved and the progress being made toward their solution; determine the final personnel strength and organization of the medical directorate, with special attention to the training division, and prepare the final, over-all training and operations plans for the director.

Training Branch.—The training branch would be charged with preparation of adequate training plans for all categories of personnel capable of absorbing technical and first-aid training; determination of the training literature and training aids that will be required; determination of which existing literature and training aids are suitable; and working out of practical training plans with the various states, professional and nonprofessional groups, professional, semiprofessional, and nonprofessional schools, fixed and field-type medical installations, and governmental and public information media, in order to insure maximum training for personnel of all categories, to include the general public.

Equipment and Supply Branch.—The equipment and supply branch would determine the items of equipment and supply and amounts thereof to be provided each type of field unit, as well as the amounts to be placed in strategic storage; prescribe storage, stock record, rotation, and inventory procedures; determine suitable packing and crating specifications; and devise methods to insure against deterioration of stocks in storage and against loss through fire and pilferage.

The professional division chief and his deputy are the master planners insofar as casualty and noncasualty care, preventive medicine, and public health matters are concerned.

Medical Care Branch.—To assist these planners, a medical care branch would be established, consisting of those medical specialists required to determine principles and practices which would be followed to insure the best possible care to the greatest number after a nuclear disaster. Additionally, the medical care branch would determine recommended priorities for treatment, the recommended employment of medical personnel, and, in conjunction with the allied professions branch and the plans branch, the recommended employment of allied medical personnel. Proposed training programs for medical and nursing personnel would be prepared and submitted to the training branch for incorporation into the final programs. Plans for obtaining, preserving, shipping, and use of whole blood, blood derivatives, and plasma volume expanders would be the responsibility of the medical care branch.

Allied Professions Branch.—The allied professions branch, in conjunction with the medical care branch and the operations division, would determine the recommended employment and training of the various categories of paramedical personnel. This branch would also be charged with determining which laws and statutes currently interfere with the adequate training of paramedical personnel and, in conjunction with the legal adviser, devising ways and means of having such laws suitably amended or repealed.

Public Health Branch.—The function of the public health branch would be the preparation of plans to insure the continued health and physical stamina of the large numbers of uninjured, both prior and subsequent to a thermonuclear attack. This is a problem of very great scope. A medical intelligence officer is included in the public health branch for the purpose of keeping all members of the medical planning group apprised of those developments in nuclear energy which have medical implications and which either have not been published or have been published in foreign mediums.

Biological and Chemical Branch.—Since the use of chemical and biological agents by a potential enemy cannot be eliminated, a small biological and chemical branch has been included in the planning group to prepare those operational and training plans that will insure maximum protection from and rapid recovery after the use of these types of weapons. Also, this branch would recommend the organization, functions, and missions of the biological and chemical branch of the medical directorate.

The planning group would include 29 physicians, 1 dentist, 1 veterinarian, 4 nurses, and 32 laymen—a total of 67. These figures, at first glance, or to the uninformed, may seem large. They are not as large as the problems to be solved by the medical planning group, however. Without a planning staff adequate in numbers and quality, the plans devised thereby will be faulty or inadequate.

Role of the Medical Profession

The task force studies have indicated that the national allied medical and related associations are very much interested in the part they might be called on to play in the medical care of casualties and noncasualties after a mass attack on the United States. These studies have also indicated the willingness of those associations to follow the lead of the A. M. A. as the representative of organized medicine in developing a national medical program. The studies, furthermore, indicated a dire need for a medical organization in a top level federal agency engaged in civil defense planning with a similar need for a complementary organization within the medical and allied professions.

Provision has been made for the participation of the medical and allied professions as well as the other related professions in the planning phase. A medical advisory council proper, consisting of nine physicians who are members of and appointed by the A. M. A., would be in a position to wield great influence not only on the government but on its own members and nonmembers of the medical profession.

At no time in history has such a challenge been presented to any professional organization as that currently posed on medicine by the threat of an all-out war involving the continental United States. Not only is it the duty of organized medicine but it is the right and privilege of physicians in the United States, through the A. M. A., to assume the lead in advising the government on plans for both preventive and curative medicine to be implemented in case of national disaster. Undoubtedly, the medical profession is willing to assume the leadership in solving the multitude of problems involved. Certainly, the allied medical professions are looking to the A. M. A. for such leadership. A full-time staff is considered an essential element of the advisory council.

The functions of the council would be to provide advice to the director of OCDM and to the director of the medical planning group on all phases of disaster and survival medicine, national medical organization and functions, national medical plans and policies, field medical organizations, their employment and equipment, utilization and training of medical and allied health personnel, training of all segments of the population, medical equipment and supplies, public health, preventive medicine, and welfare matters, medical aspects of chemical, biological, and radiologic warfare, and communications and transportation required to support the medical efforts.

Such advice would be given when sought by either of the directors, when new material should be made known to either of the directors, and when material published or about to be published by the planning group is not in keeping with policies and principles of the A. M. A. or the high traditions of the medical and allied professions.

To assist the council would be six advisory committees, each consisting of experts in their fields, appointed by their parent national organizations at the invitation of the A. M. A. These committees would work on problems pertinent to their fields, prepare appropriate studies and recommendations, and submit them to the council for its consideration. Material approved by the council would be transmitted to the director of the medical planning group through the director of the OCDM for incorporation into plans, procedures, or policies, as appropriate. When accord between the council and the planning group is reached, such material would be translated into policies for dissemination by the A. M. A. through state and county medical societies to members and other professional and interested organizations.

With such an organization in being and functioning, not only would the federal government feel secure that its medical plans and policies were feasible, proper, and sound but organized medicine and all allied interests would also feel secure that the steps taken by the federal government to prepare for an eventuality were the best possible.

Further, the A. M. A. would be providing the leadership and guidance so sorely needed, would be in a commanding position insofar as solutions to national disaster medical problems are concerned, and would be assuming its rightful role not only in this important phase of medicine but also in the very survival of the United States.

In all previous wars, while the medical profession has been an important adjunct to combat and military activities it has nonetheless been no more than an adjunct. In the future all-out, mass-type warfare, plans for employment of the medical and allied professions prior to combat and the effectiveness with which their skills and resources are applied immediately afterward will determine whether the nation lives or dies.

Medical Directorate

The organization of the medical directorate is a much more extensive establishment. While the medical planning group was made up of a number of planners, free of preconceived ideas and stereotyped thinking and with missions that will probably require two years to complete, the medical directorate is designed to be a permanent body, so organized and staffed as to execute the operational and training plans of the predecessor organization and prepared to supervise and direct the nationwide medical service in the event of a national disaster.

The broad functions of the medical directorate would be to maintain current the estimate of the medical situation in the United States; maintain current the estimate of the medical requirements necessary to support the United States in case of a national disaster; maintain current the estimate of the medical resources available in the United States; maintain current the operational plans which, on implementation subsequent to an attack of any type on the United States, will provide the greatest amount of medical care to the greatest number; be prepared to execute prepared national medical plans and policies; maintain current the training plans which will insure that all segments of the population of the United States are prepared psychologically for an all-out attack and are prepared to assist themselves and others through the provision of self-aid and first-aid and that those groups with the potential are prepared to assist the health professions in the care of the surviving casualties and noncasualties; carry out the training plans formulated by the medical planning group; maintain a complete, up-to-date, detailed listing of medical and allied health personnel in the United States to permit an immediate mobilization in case of disaster; determine, procure, allocate, disperse, store, and maintain records on and surveillance over the medical supplies and equipment, including first-aid supplies, required to provide medical service to the surviving casualty and noncasualty population of the United States after an all-out attack; determine and promulgate the policies and principles pertaining to disaster medicine that will insure maximum care to the greatest number within the means available subsequent to an all-out attack; determine ways and means and promulgate policies and principles that will provide the maximum protection against and the most rapid recovery from the effects of chemical, biological, and radiologic warfare agents; determine ways and means and promulgate policies and principles that will insure maintenance of the highest possible state of health, well-being, and morale of the uninjured surviving population; be prepared to establish a statistics and medical records office; supervise the activities of the medical sections of the regional offices; maintain liaison with those professional associations, agencies of the federal government, educational institutions, and industries whose activities have an impact on medical civil defense; and obtain, evaluate, and collate information pertaining to all aspects of mass weapons having medical implications and generate medical intelligence.

The medical directorate would be organized and become functional immediately on accomplishment of the missions assigned to the medical planning group. The reason is twofold: (1) to initiate execution of the plans devised by the planning group and (2) to have in being an organization ready to function in case of war.

Space does not permit a detailed description of the medical directorate, its personnel requirements, and its functions. Furthermore, the detailed planning for this organization is properly the function of the planning group, based on its estimate of the over-all situation.

Conclusions

I wish to emphasize that if an adequate medical service is to exist and be ready to function when required, a coordinated and comprehensive effort by an adequate staff to develop and implement a feasible plan is an immediate essential. The problem of health and medical care in the nuclear age, when living casualties after one attack may number millions, when medical resources probably will not be adequate to cope with the overwhelming numbers dependent on those resources, and when every individual who has a potential for work must retain that potential or have it restored to him at the earliest practicable moment in order that he may return to some form of recovery activity, is the most serious and vital problem that the United States, and especially organized medicine, has yet faced. Without a planning effort and a training effort in keeping with the magnitude of the problem, the recovery after an attack on this country, and even the life of the country itself, is in serious jeopardy. I believe the plan presented will meet the requirements of the situation.

OPERATION STAR

Burton E. Adams, M.D., San Leandro, Calif.

Shortly after 6 p. m. on Friday, June 20, 1958, Alameda and Contra Costa counties in California began picking up the pieces that remained from the largest disaster ever to strike the area. A simulated earthquake equivalent in force to the famous San Francisco quake of 1906 rained death, destruction, and ruin on the two heavily populated areas. By the time the count was completed, casualty figures ran to well over 3,000. The total number of dead had not been tabulated since the full disaster relief effect of both counties was directed toward emergency collection and treatment of the injured. Within the four-hour period from 6 p. m. until 10 p. m., a total of 2,100 simulated casualties had been collected at a dozen disaster sites and collection and sorting stations, given first aid and emergency lifesaving treatment at these locations, loaded into innumerable moving vans and mass transportation vehicles, and taken to hospitals in the bicounty area where they were provided with definitive medical treatment.

The operation was completed successfully only because some 3,000 persons took an active part in the disaster relief operation, all 24 hospitals located in the two-county area participated under their individual sector commands as did civil defense personnel of both counties and from all necessary services, and, last and most important of all, intensive planning had preceded the operation on all levels.

The best way to give you a picture of what was involved would be to follow the steps leading up to the actual exercise, describe the operation itself, then point out some of the lessons learned, both good and bad—what worked, and what did not work.

Preplanning

Operation Star culminated five years of work by the disaster committee of the Alameda-Contra Costa Medical Association headed by Dr. Wayne Chesbro. It began with stimulating the formation of concrete hospital disaster plans put to the test force by Operation Medic involving one hospital in Berkeley in 1956, then Operation Pill Hill involving five hospitals in Oakland in 1957, and an actual disaster by an explosion in a ship at Todd Shipyard, with 40 casualties. This was preliminary training.

The definitive planning for Operation Star started five months ahead of the actual test operation. General ideas regarding its purpose and scope and the nature of the test exercise were discussed and agreed upon by the committee.

The major objectives of the exercise were as follows: (1) to offer training to the medical and technical personnel of the disaster site sorting stations and the respective major hospitals of Alameda-Contra Costa counties in the initial care of casualties from a major catastrophe of local nature and the eventual and definitive care of such casualties in the major hospitals; (2) to demonstrate the adequacy of medical planning and the coordination of such planning for large-scale local disaster by the Alameda-Contra Costa Medical Association; and (3) to invite observation and evaluation of such demonstrated planning by official civil defense personnel of local, county, state, and federal levels, as well as members of the Council on National Defense of the American Medical Association and the armed forces.

Next, the nature of the disaster was discussed. Up to this time much of our planning had been with an atomic blast in mind. However, such a catastrophe tends to make an individual feel hopeless in the situation. Either you have "had it" and you will not need to worry, or it missed you and the catastrophe is so great that as an individual you cannot do much about it except to evacuate. These subjective feelings engender a lethargy and a feeling of "what is the use of working anyway, when there is a good baseball game I could go see?"

However, in California an earthquake is a very real thing. In the San Francisco Bay area, history is related to two events: the gold rush or the earthquake and fire of 1906. A major earthquake fault line runs through Alameda and Contra Costa counties, and one or more times a year we pick up the paper to read that a tremor of magnitude x was recorded or perhaps we are standing in the living room and hear a rumble and feel a shake. We look out to see if a truck is going by, then look up to watch the chandelier swinging and to see if there are any more cracks in the plaster. Thus, we are conscious of earthquakes, and I personally have seen the results of the Santa Barbara quake of 1925 and the recent Tehachapi quake.

For the reason, then, that such an earthquake is an ever-present possibility in our area, it was decided to use a large quake of Richter magnitude 9 as the destructive force. Moreover, an earthquake could realistically be expected to cause disruption of utilities as well as destruction of industries which routinely carry on all manner of chemical, biological, and radiologic processing operations. Here was an instrument for creating casualties from physical trauma, chemical and heat burns, smoke and fume inhalation, acute psychological trauma, and radiologic contamination.

Member, Committee on Civil Defense, Alameda-Contra Costa Medical Association.

Once general plans had been made, we soon found it necessary to expand representation at the Alameda–Contra Costa Medical Association meetings to include the following groups, to whom specific assignments were given: civil defense directors, sector chiefs, disaster chairmen of individual hospitals, women's auxiliary, military representatives from department of defense installations involved, American Red Cross, Boy Scouts and rangers, hospital labor councils, and news media.

After the initial meetings called by the Bicounty Medical Association Disaster Committee had familiarized the major participating agencies with the suggested format of Operation Star, detailed planning was further carried on by civil defense and Medical and hospital representatives in their local jurisdictional areas. Over-all coordination of the bicounty program was effected by repeat meetings of the Medical Association Disaster Committee with attendance by representatives of local government. The 20-minute motion picture "Operation Pill Hill," which recorded the salient portions of the earlier disaster drill involving five hospitals (four on one hill) in Oakland, Calif., was shown repeatedly to groups intending to participate in Operation Star. Copies of the film, produced by the Alameda–Contra Costa Medical Association, were made and retained for use and loan by the Oakland Civil Defense and Disaster Organization and the California Department of Public Health.

Although all local planning for the big drill did not necessarily follow a strict pattern, the detailed local plans for participation in Operation Star generally consisted of two major coordinated efforts.

Local Participation.—The first effort was toward community-wide coordination of all civil defense and sector chief medical and health service participation. This involved alerting transportation, communication, law enforcement, medical and health, and ancillary personnel. In many cases, additional volunteer recruitment and training was necessary. The sector chief medical services and local civil defense organizations decided on the location of disaster-site sorting stations within their areas. In most cases public parks or school grounds were selected which were more or less equidistant to the hospitals to which they were to send patients. There were 12 disaster-site sorting stations actually used during the test. Although local areas varied somewhat in communications arrangements, the over-all plan was for each disaster-site sorting station to communicate directly to local respective area police radio control centers (generally by short wave radio) and from there by telephone to the Alameda–Contra Costa Medical Association Headquarter Control Center. In the Oakland area, a further refinement of this plan included radio contact by handie-talkie units between the triage command post at the disaster-site sorting station and the individual medical teams dispersed at the disaster site providing field first aid to casualties.

Casualty transportation was quite realistic and consisted of large moving vans volunteered for such use by local commercial transportation companies. As many as 15 casualties could be taken (without stacking litters in the van) to one hospital all at one time. Such forethought not only made it possible to deliver rapidly large numbers of casualties for definitive treatment (with a minimum of transport involved) but also imposed "surge loads" of casualties on the receiving hospitals. It was believed that such an arrangement more nearly approximated actual conditions in a large-scale disaster, in that it required the handling of large numbers of casualties at one time rather than one at a time which occurs upon arrival of an ambulance or automobile.

Hospital Participation.—The second major local effort was undertaken by each of the hospitals participating in the exercise. Several of the 24 hospitals held preliminary drills in anticipation of the big quake. Each of the 24 reviewed, wrote, or rewrote its hospital disaster plan with an eye toward bringing the plan up to date and familiarizing the staff with the plan.

It is worthy of note here that only the most cooperative attitude was evidenced by all hospital staffs involved. It is, however, felt by some that recent changes in the requirements of the Joint Committee on Accreditation of Hospitals (The Journal, Jan. 18, 1958) assisted materially in pointing up the necessity for adequate hospital disaster planning.

The Test

With preliminary planning for the exercise in the background we will attempt to give an account of what actually occurred during Operation Star without too much detail as to the line of authority involved.

Shortly after 6 p. m., casualties began arriving at the disaster sites. The casualties consisted of Boy Scouts, members of community civic and social groups, and families of participants. They were tagged with emergency medical tags on which diagnoses had been previously written, and small teams of first-aid workers and nurses under doctors' directions went to work providing appropriate lifesaving and first-aid techniques. A command post was set up at each disaster site. These varied as to how elaborate they were, based on the equipment available. Characteristic, however, was the one at Lakeside Park. A message center was set up with short wave radio communication to the supporting hospitals and the Alameda–Contra Costa Medical Association disaster center. The telephone company ran in an emergency line, but it was soon swamped with calls. A loud speaker system helped to direct local activity. Subchiefs for supply and transportation assumed their duties. Statistics on available hospital beds were rapidly gathered and kept current during the exercise. Casualties were rapidly treated and loaded on trucks to be transported to designated hospitals.

The hospitals were alerted shortly after 6 p. m. and began calling their disaster teams. The methods for notifying personnel to report to the hospital varied, but generally each department head or his representative on duty was responsible for calling in members of the department. Doctors were called either by a special message center operator or by notification of the local telephone answering service which called doctors on a previously prepared list. In a disaster of this magnitude, notification of personnel would not be necessary for they would be immediately aware of the need and report to their stations for duty. However, means for assembling people in case of small scale disasters should be ready.

The individual hospital plans varied from four pages of brief description and diagrams to small volumes. The way the hospitals approached the problems also varied. Some played it "cold" with no prior warning or preparation by the general staff. Others had elaborate previous drills and critiques so that a smoothly working organization was ready. Also, the extent of play varied. One hospital handled 500 casualties, going only through the triage phase. Others went to the "dirty sheet" stage, setting up operating rooms, simulating infusions and transfusions, and holding time schedules as close to the actual as possible. Some received only a few casualties to try out their flow systems, and others handled casualties almost equal to their total bed capacity.

Hospital plans are not part of this discussion, so let us proceed to the activities at the Alameda–Contra Costa Medical Association command post. The first problem was that of communications—setting up a message center to handle both radio and telephone messages with runners locally. Concurrent with this was the dispatching of the small army of observers and preselected monitor umpires. Since both of these groups reported to the headquarters at the very beginning of the exercise, it was possible with use of an outdoor public address system (there were too many to handle adequately inside) to give last-minute instructions as to what was expected of them. Each person was given a pin-on identification tag which indicated by color and nomenclature whether he or she was an observer or a monitor-umpire. Each was also given a form to fill out on his observations and criticisms. The observer's form was a single sheet asking for constructive comments on the exercise and indicating the observer's name, position, and area and/or hospital observed. The monitor-umpire form consisted of seven pages of mimeographed questions (79 in all) covering the many aspects of hospital operations in the care of mass casualties. These persons were transported to their destinations and back by Navy buses and cars furnished by the Association's women's auxiliary. The bicounty command post had established a "control board" composed of representatives of the various disciplines involved in the medical and health control activities. A veterinarian, dentist, pharmacist, mortician, and public health officer were on the board. Technical questions arising during the exercise were referred to the specialists involved. Problems on whole blood, narcotics, disposition of the dead, and similar items were consequently handled with dispatch at the command post. By adequate preplanning, disposition of the dead was adequately cared for from the legal standpoint. Under an over-all coroner coordinator, deputy coroners previously assigned were stationed at respective disaster sites and hospitals.

At the command post, a running record of the bed census was kept and coordination of the blood supply was carried out. Also, several preplanned special situations were initiated. One of considerable interest was the transportation by Army helicopter of blood and a neurosurgical and vascular team from central Oakland to an outlying hospital and the return with a load of casualties.

Results

Now, what were some of the lessons learned? Most important was the lesson learned by each participant of what such a situation might be like and what role he could play so that the next time he would do it with less confusion and better. For example, the registrar at one triage area had nice tables and chairs set up so that the casualties could come up to her desk and be registered; she had to be told that she should go to these litter cases instead of their going to her.

The procurement of casualties is vital to such a problem. Boy Scouts were our best source. They played their parts well, and their enjoyment and enthusiasm stimulated all who came in contact with them. They unanimously considered it a "blast" (not in the atomic sense) and were generally sorry when it was over. Doughnuts and cider or coffee served by the hospitals were joyously received and helped to provide fond memories and repeat volunteers. Also, their used dressings and emergency tags were cherished souvenirs.

Ambulant patients at the Veterans Administration Hospital and the Oak Knoll Naval Hospital provided these plans with casualties. Organizations participating in the community function as a group were another good source of patients. One such, the "Chanticleers," a little theater group in Castro Valley, were especially good in not only furnishing numbers of patients but, as might be expected, playing their roles to the fullest as psychopaths, dead and dying, and persons in pain. Moulages added to their reality, and some wore old clothes over bathing suits so that the clothing might be actually cut away to treat their extensive injuries. Also in evidence were families of hospital personnel, and one county hospital recruited 200 casualties from such a source. The families of participating doctors were poor sources of casualties, but the most unreliable of all were civil defense volunteers who had signed up ahead of time to act as casualties. At one disaster site, only 6 of a promised 50 from such a source actually arrived at the hospital. Another source is the disaster-site personnel who, when the action at their posts slackens, can become casualties for the hospitals to work on. A lieutenant in charge of a group of sheriff's reserves became such a casualty involuntarily and was given the full treatment clear to the morgue, much to the enjoyment of many, before his boys unlocked the handcuffs which held him bound to the litter.

One of the outstandingly good lessons was the enthusiasm displayed by the participants. Many factors contributed to this. The type of exercise selected, an earthquake, made everyone realize the importance of what he or she was doing, for this might be for real tomorrow. A tornado would probably play the same role in the Middle West. Also, the play was not forced on anyone. Here was the opportunity for a coordinated effort, and everyone could play an important role as he saw fit. However, frequent meetings stimulated the laggards by showing what others were accomplishing and planning. Friday evening was selected as being the least inconvenient time for everyone. Its occurrence just before an A. M. A. convention assured us of observers of national importance and also helped to stimulate interest. The novel participation of a helicopter did the same, as did the assurance of photographic and news coverage. These, plus many little factors, stimulated an enthusiasm that was a pleasure to see and bespeaks well for future exercises.

Many specific deficiencies were brought to light. For example, the importance of alternates for commanders of the various units was brought out when one hospital coordinator declared himself a casualty. Some hospital elevators will not accommodate the civil defense stretchers. First-aid stations should be outside a hospital proper. Participants with specific jobs should have labels. Triage areas must be large enough. The physician in charge of triage must be one of the best-trained men in the hospital.

These and other points were brought out by the participants and the comments of the monitors. Within another month we hope to have put together scenes from this exercise with those of the previous movie on "Operation Pill Hill" to create an instructional movie for further training of our own as well as any other group which may want to borrow it.

We hope from these remarks that you may be stimulated to hold a similar test. Certainly one learns by doing, and nothing talks as well as actual performance.

OPERATION AFTA

John K. Hampton Jr., Ph.D., New Orleans

On the evening of March 21, between 6:30 p. m. and 1 a. m., Tulane University carried out a realistic drill exercise. During the afternoon of March 21 a symposium was held on disaster medicine and included briefing discussions pertinent to the exercise to be conducted that evening.

The purpose of the drill exercise was to provide a realistic situation for instruction of medical students in the principles of disaster medicine. Also, the resources of the campus were used to demonstrate the need for adequate paramedical services in carrying out a rescue mission. The exercise had been so designed that it would adequately test the facilities of a 200-bed Federal Civil Defense Administration portable emergency hospital which was on loan from Baylor University School of Medicine. Finally, such an exercise, carried out effectively, provided proper emphasis to the need for community preparedness.

The basis for the disaster was a simulated crash of an airplane of large size onto the campus between Richardson Chemistry Building and Richardson Memorial Medical Building. This crash occurred about 6:30 p. m., March 21, and caused "fire" and "physical damage" to both buildings. This warranted the assembly of search and rescue personnel and the mobilization of the emergency hospital. About 7 p. m., one-half hour later, a secondary "explosion" of the fuel system of the airplane caught accumulated spectators by surprise, creating an additional large number of injured. The "explosions" and the attendant "fire damage" were realistically portrayed by lighting, sound, and smoke-generating systems. About 150 casualties were created by the initial "crash" and about 350 by the secondary "explosion."

The casualty group was composed of approximately 200 students from the second and third year medical classes and approximately 300 from the general student body. These casualties had been

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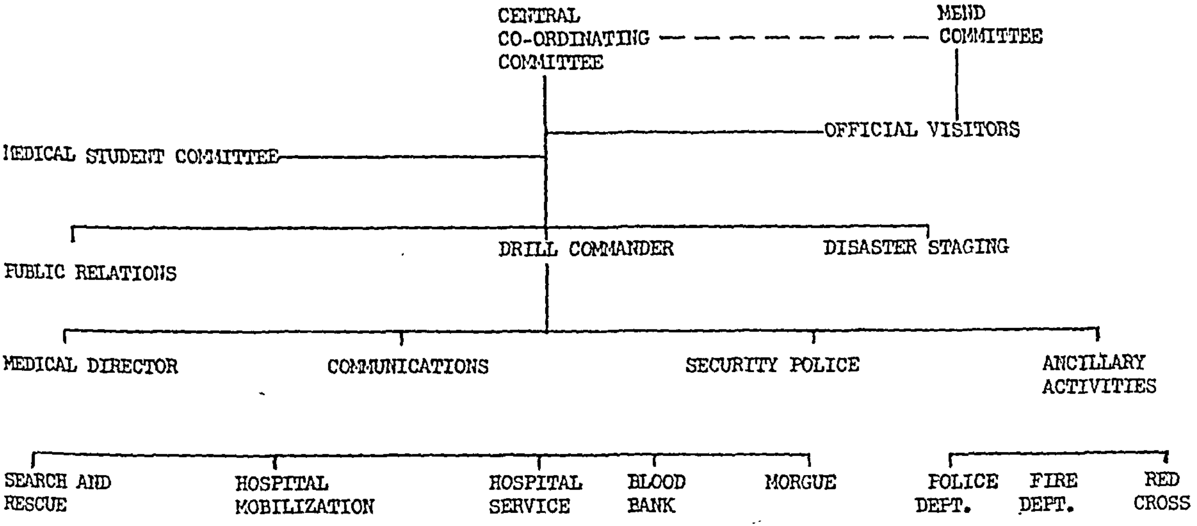
Associate Professor of Physiology, School of Medicine, and MEND Coordinator, Tulane University.

assembled earlier and their injuries realistically made up by modern casualty simulation techniques. The realism of these techniques was sufficient so that only by closest inspection could the lack of reality be detected. Portrayal of behavior appropriate to distress, emotional disturbance, and inability to speak and see was emphasized.

Upon notification of the disaster, the search and rescue mission was put into action. This group was composed of first-aid teams, the members of which were fourth year medical students, and litter bearers from first year medical class. Their duty was to seek out and administer appropriate first aid to casualties and to organize a system for transporting casualties from the point of injury to the emergency hospital. The emergency hospital was brought to the campus by a team of students who had been previously trained in its operation.



Organization plan for operation AFTA.

The hospital is functionally packed in two large moving van trailers in color-coded boxes. The hospital consists of 200 beds (army cots) and has sufficient supplies to divide these into five or more appropriate hospital wards. Also, three surgical rooms, admission triage and first-aid facilities, clinical laboratory, and pharmacy and x-ray facilities are provided, and the hospital is equipped with central supply and sterile supply.

Upon receipt at the hospital, the patient was properly inspected and sorted according to the nature of his injury. Disposition of the dead took place in the morgue. Disposition of walking wounded persons who did not require hospitalization was effected by either self-help or minimum help, and such were immediately discharged from the triage station. Those requiring hospital admission were directed to the appropriate hospital unit, such as surgery or shock ward. The hospital was staffed by the hospital services group. This group consisted of clinical faculty members of the medical school who filled key professional positions. Most "physicians" were senior medical students, each of whom had a clinical advisor from the faculty. Nurses were recruited from the community, and each had a nursing student as a preceptee. Nurses aides were played by nursing students. Orderlies and ward men were selected from the first year medical class, and clerk-typists were selected from the student body and university clerical personnel. The hospital service personnel had all been assigned in advance, and each, according to the role played, had proper information supplied to study for his responsibilities during the drill exercise.

A minimum amount of "faking" of medical procedures was permitted. For example, patients going to surgery were properly prepared and draped and surgical staffs were scrubbed and gowned. The operating room equipment was conventionally packed and sterilized and was not reused in the exercise without being repacked and actually resterilized. Bandaging, application of casts, and taking of x-rays were also carried out realistically. In addition, conventional civil defense emergency medical and hospital records systems were employed throughout the exercise.

Since the exercise was carried out as a university function, its program was under the administration of a central coordinating committee. The general organization can be determined by reference to the figure.

All participants in the exercise wore appropriate identification. However, observers to the drill exercise were encouraged. Uniformed cadets of the ROTC program served in a security policing system which provided actual patrol of the campus for misdemeanor or misbehavior and established a security policing system for the drill exercise itself. The latter consisted of a cordon of traffic lanes and the security of the disaster and hospital areas. Thus, persons without proper authority to enter the restricted areas came under control of the security police. A communications system was also set up to provide adequate contact between all units. Several students who were experienced amateur photographers were assigned to take extensive documentary photographs during the drill.

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THE PROFESSION'S CIVIL DEFENSE RESPONSIBILITIES

Gunnar Gundersen, M.D.

It is an honor for me to participate in this civil defense conference, and I am delighted that you invited me. I always consider it a pleasure to meet and talk with dedicated individuals. Yes, I think of you as dedicated—serving a cause in which the American people generally are complacent and apathetic. And, I'm sorry to say, many medical and health personnel share this complacency and apathy. But you, by your very presence here, demonstrate that you are indeed laboring in the service of mankind.

One of my last duties as president-elect of the American Medical Association was to address the Sixth Annual National Medical Civil Defense Conference in San Francisco sponsored by the A. M. A. Council on National Defense. It is at meetings such as that one—and this one here today—that the responsibility of the medical profession in civil defense affairs is manifested. And that is what I want to talk about briefly today—the medical profession's civil defense responsibilities.

The diligent and sustained work which is being given to civil defense by the A. M. A. is not a new activity of organized medicine. Nearly 13 years ago, the A. M. A. appointed a special committee to study emergency medical services during war or grave national emergency. The medical profession was aware of the problem and alert to the need for its solution fully five years before the federal government enacted civil defense legislation.

The Association is most fortunate in having such experienced and energetic physicians to serve on the Council on National Defense and its Committee on Civil Defense. Through them, the Association has followed a positive, realistic, and sustained policy of active participation in medical civil defense affairs.

The 85th Congress provided for greater federal leadership and financial assistance to the states in the development of civil defense plans and preparations. The change in the declaration of policy in the Federal Civil Defense Act to make the responsibility for civil defense a joint one between the federal government and the several states and their political subdivisions is indeed a long-awaited and much-advocated step in the right direction. But, of course, only time and future meetings of Congress will determine its implementation and consequent effectiveness.

Mass Emergency Care

Meanwhile, the average individual physician and his role in the larger civil defense picture is of paramount importance. Usually, a physician thinks of emergency medical care in terms of treating one person. However, it seems to me that if the profession is to discharge its responsibility effectively in any disaster situation the thinking of such physicians must be reoriented. Medicine must think in terms of providing emergency service on a mass basis.

I know that your efforts have been in that direction. You know the value of proper collection, evacuation, sorting, admission, and reception of patients to medical facilities under disaster conditions. Each group involved in this process—the rescue and warden, transportation, and hospital clerical services—look to the physician for proper medical guidance in their work. Physicians who work with such groups are rendering services equally as valuable as the surgeon in the operating room. All are important members of the medical team.

Medical service rendered in an emergency differs from that in civilian practice. The assignment of priorities for care is a most important medical duty. As such, it should be performed by the most experienced physician on the scene. Here judgment must be exercised to a degree the physician seldom is called upon to make.

President, American Medical Association.

How can he gain experience? Certainly he must be trained before a real emergency occurs. Therein lies the value of test operations, dry runs, or CPX's. I was most gratified to learn that one feature of this two-day program was the reports on the experience gained from three test exercises. Simulated disaster conditions, such as in those test exercises, offer a variety of medical and surgical problems that will test the physician's judgment. This is most important, as improper sorting can lead to inadequate medical service.

As you know, every effort must be made to give the best possible medical care under the existing circumstances. This is difficult, because in disaster large numbers of patients urgently require the services of too few medical and allied medical and paramedical personnel, inadequate facilities, and too little equipment and supplies. Nevertheless, the physician must do all he possibly can for each patient. Therefore, the responsibility of the medical profession is to accomplish the greatest good for the greatest number within the framework of sound medical and surgical techniques. This can be done if the physician works calmly and efficiently. But to do this he must be trained in advance of the event. The profession's ultimate responsibility is its own preparation to meet the emergency.

Thus, the thinking of many physicians must be reoriented if the profession is to discharge efficiently its civil defense responsibilities. They must be cognizant of their responsibility for the total care of all the wounded or injured patients.

I believe that it is you who must inspire, convince, cajole, or prod other members of the profession to accept their responsibility in any emergency situation. It is only by the establishment of a broader base of participation by the profession in civil defense affairs that medicine will not be found wanting when disaster strikes.

Natural Disasters

And disaster does strike. I speak now not of the nuclear or thermonuclear holocaust but of natural disasters. In the past few years our civilian population has experienced an increasing number of natural disasters. Floods, fires, explosions, tornadoes, and other disasters have occurred in all parts of the United States, causing death and injury to many persons. Usually, the local communities or large geographical areas have floundered under the impact of the disaster.

One insurance company reports that natural disasters were responsible for more than a third of the deaths in catastrophes—accidents in which five or more persons died—during 1957. Deaths in catastrophes in the United States totaled almost 1,700 during that year, or about 400 more than in 1956. The increase was largely a reflection of the unusually heavy loss of life in hurricane Audrey, which caused about 350 known deaths early in June, 1957, most of them in Cameron, La.

In addition to the hurricane, there were four other major catastrophes—those which caused at least 25 deaths—during 1957. Fire destroyed a home for the aged at Warrenton, Mo., causing 72 deaths; a tornado struck the Kansas City area killing 39 residents; a gas explosion killed 37 men in a coal mine near Bishop, Va.; and a March blizzard killed 29 persons in the Great Plains states. As a result of these four disasters and hurricane Audrey, the loss of life in natural disasters during 1957 was the highest in nearly 20 years.

Many costly but important lessons have been learned as a consequence of these disasters. We know now that the communities that had adequate medical and hospital disaster plans were prepared to cope with the disaster more quickly, effectively, and efficiently than the communities without adequate plans. Those with partial or incomplete plans, although inadequate, fared better than the communities without any plans or preparation.

Leadership of the Physician

These disasters have clearly demonstrated the paramount need for preplanning and preparedness. They have shown that hospitals, physicians, paramedical personnel, and others must cooperate and function as a team. They have shown that a team plan requires close coordination and integration. But, most importantly, disasters have shown that a team needs leadership.

I believe that every physician has a responsibility to prepare himself and to participate in disaster planning in his community. Nurses, paramedical personnel, hospital clerical personnel, ambulance drivers, rescue workers, and others will look to the physician for guidance in the performance of duties in the disaster situation. It is the physician who must coordinate the activity of these persons. The physician must weld them into an efficiently functioning medical team. This means, of course, that the physician must enlarge the scope of his thinking and responsibility. He can no longer confine himself to the narrow sphere of his own professional problems. He must furnish guidance to health and medical and ancillary personnel that will assure optimum participation and results.

And again we come to the question: how can this best be done? I say it will be done when the physician recognizes his responsibility. So, again, I ask you who are today the dedicated people of the profession in civil defense to go back to your home towns and inspire, convince, cajole, beg, or prod the members of the profession to accept their responsibility.

NATIONAL SHELTER PROGRAM

Paul S. Parrino, M.D., Battle Creek, Mich.

This statement on the national shelter program will be presented primarily as it relates to our interests as medical people. But I would like to begin with a brief summary of the latest official statement by the Director of the Office of Civil and Defense Mobilization on May 7, 1958. Governor Leo A. Hoegh outlined five things which the administration will do in connection with the "National Policy on Shelters."

First, it will try to bring to every American all of the facts as to the possible effects of nuclear attack. It will try to inform every American of the steps which his state, his local government, and he can take to minimize these effects. To do this, it will expand substantially defense programs for information and education.

Second, the administration will itself initiate a survey of existing structures on a sampling basis. This survey should enable it to assemble definite information on the capabilities of existing structures to provide fall-out shelter. There are many facilities, especially in larger cities, and in mines, subways, tunnels, and cyclone cellars, which already afford some fall-out protection. It is necessary to determine accurately how much protection they afford in order to be able to use them properly.

Third, the administration will accelerate research to show how fall-out shelters can be incorporated in existing or new buildings and will work to design types which are most economical and most effective.

Fourth, the administration will, as soon as funds are available, construct prototype shelters suitable for different geographic areas and for different climates. It will test the prototypes through actual occupancy by people and through incorporating such shelters in underground parking garages, understreet shelters, subways, schools, hospitals, industrial plants, commercial buildings, family residences and apartments, and other buildings in the several states.

Fifth, the administration will provide leadership. It will set the example by incorporating fall-out shelters in appropriate federal buildings yet to be built.

The strong emphasis on shelters to provide protection from radioactive fall-out is extremely satisfying to the Biophysical and Medical Sciences Office. We are keenly aware of how much of a hazard radioactive fall-out can be with thermonuclear weapons. We have estimated how tremendously fall-out could increase our medical case load in the immediate and longer range postattack period. And we welcome anything which will help lessen the possibilities of such a load.

Background

Our concern about the hazards of radiation goes back to the days of the old Health Office under the Federal Civil Defense Administration. As far back as 1952, technical bulletins were published entitled "Emergency Exposures to Nuclear Radiation" (TB-11-1) and "Emergency Measurements of Radioactivity in Food and Water" (TB-11-9). But radioactive fall-out first became a matter of real concern in 1954, and it was then that the desirability of providing cover or shelter from it was pointed out. Basement shelters and underground shelters with 3 ft. of earth cover were recommended (see Annual Report, 1954, page 113).

Early in 1955, information was released that new high-yield weapons produced radioactive fall-out that was dangerous hundreds of miles from the blast. It made it evident that protective construction had to supplement evacuation both in target cities and in fall-out areas. The fall-out hazard forced us to a new approach to shelter design because of the probability that people would have to stay in shelters for several days instead of for a few hours. Minimum space allowances were increased from 6 to 10 sq. ft. per person; ceiling heights were raised; doors to keep out radioactive dust were added; and filtered mechanical ventilation entered the picture (see Annual Report, 1955, page 132).

In January, 1956, the National Bureau of Standards began a study of the attenuation of nuclear radiation by shelters. In June, 1956, the American Machine and Foundry Company began to design a 150-ft. span, reinforced-concrete dome shelter with the capacity to house about 3,000 persons for several days or longer.

With this project, the Health Office became greatly interested in the health and medical requirements to maintain the physical and mental health of those who might need to stay in such a shelter. Attention was focused on space needs for dormitories, toilets, recreational and work activities, and medical and other facilities. Attention was given to the kinds and amounts of various equipment and supplies that would be needed, including not only first-aid and other medical supplies but garbage and trash containers, disinfectants and detergents, chemicals for toilets, soaps, and a whole miscellany of essential sanitation supplies. Water requirements were planned on an austere basis for adults and also for infants and young children.

Acting Director, Biophysical and Medical Sciences Office, Office of Civil and Defense Mobilization.

The earlier technical bulletins were revised, and a special one on "Protection Against Fallout Radiation" (TB-11-19) was issued. The Health Office worked closely also with the Engineering Office, which also issued a technical bulletin relating to "Shelter from Radioactive Fallout" (TB-5-2, revised 1956). This describes protective measures for persons 15 miles or more from a potential target. It describes basement shelters, pipe shelters, ditch shelters, and culvert shelters. It discusses temporary family shelters and permanent group shelters. In May, 1958, the Engineering Office put out an eight-page technical bulletin on "Family Shelters for Protection Against Radioactive Fallout" (TB-5-3). As family men, you may be interested in seeing this bulletin. Copies are available.

This bulletin provides guidance to engineers, architects, and contractors, as well as the general public, in planning family shelters for protection against the effects of radioactive fall-out beyond the blast range of nuclear explosions. It suggests the advisability of planning for a two-week occupancy, even though in many areas radiation levels may permit leaving shelter after two or three days. It sets up a minimum desirable standard of at least 12½ sq. ft. of floor area per each occupant and 80 cu. ft. of volume. It gives desirable standards for shielding, ventilation, radio equipment, food and water supply, sanitation, and miscellaneous supplies. It shows three types of family shelters: (1) outside underground, (2) basement, and (3) above ground. It even tells where to buy ventilating equipment.

Present Plans

Our Engineering Office is at work developing and improving designs for fall-out shelters. There is no claim that any of these are perfect, but all are in process of being bettered as much as can be. These plans include improvised basement fall-out shelter, basement family fall-out shelter, family fall-out shelter, group fall-out shelter, industrial shelter, underground garage shelter, highway fill shelter, and subway tunnel shelter.

Now everyone feels that the Biophysical and Medical Sciences Office has a paralleling and collateral interest in the protective shelters which the Engineering Office is in process of designing. The health and medical interests must be factors in that design in order to ensure that people come out of those shelters alive, well, and able to function.

As we see it, it is necessary to explore the medical aspects of shelter living. This includes the biological, physiological, and psychological factors involved in living in shelters. This is necessary in order to know the vital and immediate medical problems that might arise in shelters. We need to know the effects of group living in close space for long periods of time. We need to know how the vital air components in the shelter may affect the health and life of persons confined there. We see studies here involving temperature, humidity, oxygen depletion, carbon dioxide concentration, and human exudation of moisture and odor. We need to plan for medical care for shelter inhabitants. We must determine the medical requirements for sick and injured in shelters. And we need to determine requirements to prevent and control the spread of communicable diseases in shelters.

We are aware of the fact that there might not be professional medical personnel in every shelter. Therefore, we must determine how much knowledge, skills, and abilities beyond the level of first aid we ought to disseminate among the general public so that they can do what they need to do in order to survive in the shelters. We need to know what medical and other supplies need to be put in the various shelters.

Acting on this conviction, the Biophysical and Medical Sciences Office has proposed a whole range of projects for research and development. Two of these relate to "Immunization for Shelter Occupants" and "Nutritional Requirements for Shelter Habitation." A dozen more will have angles more or less relevant to shelter inhabitants, although we consider them as more general health and medical projects. The list includes studies on the simplified treatment of burns; accelerated treatments of trauma; techniques for treatment of sick patients with a combination of burn, trauma, and radiation; rapid identification of biological warfare agents; evaluation of biological warfare decontamination procedures for skin, clothing, household effects, and physical environment; development of methods and chemicals to retard decomposition of dead bodies; control of insect and rodent vectors of disease under emergency conditions; biomedical effects of radiation and methods for decontamination of such radiation effects; underground storage problems with medical items; the missions of specific medical care facilities; management methods for shelter medical care facilities; and food supplements and food substitutes.

Public Education

Also related to shelter habitability, as well as to the general problem of health preservation under civil defense conditions, is a proposed project we are considering for education of the general public to a higher level of health and medical competence.

We feel that the general public should understand the nature and impact of fall-out and that it should see the reasonableness of the need to go into and to stay in shelters. It should be aware of the fact that, quite possibly for the entire length of stay in the shelter, people will need to take care of themselves, especially in the medical field. There just cannot be sufficient medical professional personnel to cover all shelters—especially small family shelters.

We feel now that it is of vital importance to strengthen public medical and health education in several areas, so that people can save life and maintain health among those near and dear to them in the absence of doctors or nurses. We feel, therefore, that more people should be educated—perhaps one in every family—to observe evidence of illness and/or to give care in such cases as heart disease; convulsions and epilepsy; diabetes, coma, and shock; communicable diseases; diseases due to poisons, chemicals, or physical agents; infections; and other diseases.

More persons should be taught nursing procedures and practices such as determination of temperature, pulse rate, and respiration; bed making; comfort devices and improvisations; elimination needs; lifting and transporting patients; food, feeding, and nutrition; and administration and side-effects of medicine. They should be taught nursing treatments such as enemas; steam inhalations; wet dressings, hot or cold; irrigations of eye, ear, and throat; surgical dressings; oral hygiene; and oxygen therapy.

They should be taught emergency treatment and care of open cuts and wounds; fractures, sprains, and dislocations; bruises; pressure or crushing injuries; concussion or other head injuries; hemorrhage, external and internal; burns; shock; radiation sickness; illness from fatigue, exposure, or overcrowding; childbirth; and medical and surgical complications.

More persons could be taught such managerial aspects of emergency defense medical facilities as organization for emergency care, assigning and directing others, supplies and equipment, emergency supply materials, and improvisations.

We believe these things fit right into the first point that Governor Hoegh made in his "National Policy on Shelters." This type of education in the medical area is part of what every American should know to minimize the possible effects of nuclear attack on human life and national health. It certainly will make easier his survival both in shelters and afterward when he comes out.

RESUSCITATION TECHNIQUES

Robert A. Hingson, M.D., Cleveland

During 1958, 40,000 people will be killed on the highways of the United States, 6,500 will drown, and 13,000 will die from industrial accidents and asphyxia. It makes no difference whether the injuries involve three patients in a highway accident from a 200-horsepower collision or a half million from a megaton nuclear explosion; the victims must be treated individually, promptly, and intelligently. The survival of the victims concerns us far more than the disposition or the census of the fatalities.

Of equal significance is the fact that this large number of lethal casualties represents only the apex of a much broader pyramid projecting geometrically an astounding toll of severely injured, yet salvable, patients.

Physicians frequently witness physiological asphyxia as a terminal state of debilitating physical illness. In such a setting, the asphyxial state is usually irreversible and the physician cannot correct it. In contrast, acute asphyxia frequently occurs in healthy individuals in whom physicians, or anyone else with the proper equipment and the ability to use it, may prevent a fatal outcome. This reversible type of asphyxia may result from the birth process (asphyxia neonatorum), high altitude, carbon monoxide, noxious gases, industrial or martial blast injuries, submersion, electrocution, conflagration, mechanical obstruction, or surgical anesthesia. The annual death rate from acute reversible asphyxia is conservatively estimated at 50,000.

The treatment of acute asphyxia and respiratory arrest is as definitive and clear-cut as any procedure in medical science. Fundamentally, this involves clearing the airway and intermittently introducing oxygen or air into the trachea under controlled pressure.

The Physician's Responsibilities

As a member of the rescue team in the treatment of mass casualties with many severe injuries resulting from warfare or peacetime industrial or transportation disasters, the physician in each specialty has major responsibilities:

Professor of Anesthesia, Western Reserve University School of Medicine.

First, he should work in close liaison with his surgical colleagues in correlating his activities in such a manner that the maximum number of victims will be prepared in proper sequence for surgical restoration and mobilization and transport to receiving centers. Certainly, the physician should not waste his talents relieving pain in the dying when surgeons need him to prepare the salvable victims for field surgery or transport to receiving hospitals and permanent installations. The rescue physician, too, should understand full well the meaning of triage. As a member of the team, his services are supporting and ancillary during active surgery. However, because of his special knowledge gained from a career in general practice or in the front-line of the operating room, when he is alone he might be called upon to act as both surgeon and anesthetist. Probably the general physician or anesthesiologist is better able to render total emergency surgical service than his surgical specialty colleague, since anesthesia is essential as the first prerequisite for operation. The treatment of shock, the control of hemorrhage, the transport of the injured, and the surveillance of the recovery room for 1 or 100 patients represent the areas in which he has had daily experience.

Second, the physician, in his role as guardian of the functions of the brain stem, should devote proper priority to the restoration of physiological oxygenation to victims of smoke, blast, strangulation, and obstructive asphyxia. Today it is possible to prescribe oxygen from the physician's satchel as readily as the less helpful but more dramatic intracardiac administration of epinephrine or intravenous analeptic therapy. The introduction of the Western Reserve Anesthetic machine, oxygenator and resuscitator, and escape ventilator can truly dispense oxygen from the lifesaver's pocket.

For the first time, the use of intelligent oxygen therapy in the treatment of asphyxia is possible by the layman who can be taught to maintain a clear airway in the unconscious patient and rhythmically squeeze the oxygen rebreathing bag with equipment having a total weight of less than 2 lb. This type of resuscitation can also be carried out by the use of the Denmark Schuyler resuscitator, with use of the portable nonrebreathing Ruben valve.

The misconceptions concerning adequate artificial respiration techniques championed for years by the American Red Cross and Army rescue and Boy Scout manuals have resulted in needless deaths. These have finally been exploded with proper documentation by Peter Safar of Baltimore through the introduction of double airway for both adult and infant mouth-to-airway rescue techniques. Historically, they were also championed by both Elijah and Elisha in the Bible and by Professor Yandell Henderson of Yale University. We have applied these methods with success already documented in treating both cardiac standstill and respiratory standstill. Furthermore, in our monthly lifesaving courses at Western Reserve University, under the sponsorship of the Cleveland Heart Society and Drs. Claude Beck and Robert Hosler, we have taught others these techniques for the past nine years.

The fundamental principles are as follows: 1. The normal heart wants to beat if provided with oxygenated blood. 2. Once the alveoli of the lung in respiratory arrest are properly inflated with 100% oxygen, the respiratory crisis is over. A free volume gallon of oxygen comfortably contained in a pair of adult human lungs will be sufficient to sustain life for 16 minutes. One free volume gallon of air in the lungs sustains the same person for less than three minutes. 3. Even though the epiglottis is the watch-dog of the larynx, it must not be packed over the tracheal orifice by malposition of the head on the neck or by impaction of the mandible and supports of the tongue over the airway. 4. Hypoxia not only stops the motor but it wrecks the machinery, as postulated more than three decades ago by J. B. S. Haldane. It is essential for physicians to understand and to train others in maintaining an open airway in the unconscious patient. With so many thousand casualties possible from a single blast, the medical profession must adjust its sight to the atomic, hydrogen, and jet age.

Third, the physician must take cognizance of the fact that instantaneous, predictable, reversible, surgical anesthesia can be obtained for certain types of field emergencies with a single deep inhalation of 40% cyclopropane, 30% oxygen, and 30% helium in nonexplosive, prepackaged mixtures. The use of this type of anesthesia makes possible handling of large numbers of "walking wounded" by a single team in a single day.

Fourth, the place of the blood, plasma, and plasma substitute bank must be understood, planned for, provided, and utilized. On hand already is a plasma bank in the United States worth 35 million dollars in widely distributed warehouses. Yet, even closer than the plasma banks are the multiple liters of perfectly matched blood in the lower extremities of the victims; this blood can be readily called into the central circulation with autotransfusion by lifting the victim's legs to the "L" position. In hypovolemia and in hypotension related to shock and anesthesia, this simple maneuver is lifesaving, as I have documented through years of research and writing and, more recently, as Dr. Barney Greene of Brooklyn, N. Y., has noted in THE JOURNAL. The improved normetension thus developed can be prolonged by maintaining the "L" position in transportation of the injured and by ace bandaging, reverse wrapping, and snugly applied elastic stockings.

Finally, the physician must constantly seek to develop and intensify his understanding of physiology as well as pharmacology. He must remain resourceful, adaptable, companionable to both patient and surgeon, and compassionate in the application of both his humanitarian art and his scientific skills. He should share his knowledge in active programs of education of lay resuscitation personnel: civil defense teams, firemen, police, Red Cross workers, life guards, orderlies, military corpsmen, and Boy Scouts. For the past five years in Cleveland, I have had the privilege of directing such educational programs among all of these groups. It has been my experience that the physician can multiply his lifesaving service in major disasters through developing technical proficiency with understanding of principles among these groups.

Conclusions

Almost every day in our hospitals we apply these methods to patients who stop breathing or breathe too shallowly during an operation, to patients who have been relaxed and intentionally made apneic for electric shock for mental disease, and to newborn babies or to mothers who are sluggish in their breathing. Almost every day lives are sustained by an expert team of anesthesiologists who are at the same time testing and amassing data and lifesaving knowledge. This must be passed on to rescue squads at every police, fire, civil defense, and martial rescue station throughout America and our far-flung overseas bases, if any appreciable number of the thousands of people are to be saved who may, sooner than we think, have the wind knocked out of them in the oxygen desert of a nuclear or industrial blast. Oxygen sustains life. Oxygen saves life.

THE ROLL OF DENTISTRY IN CIVIL DEFENSE

Russell W. Bunting, D.D.S., Battle Creek, Mich.

In any medical preparedness program for national disaster, the development of allied medical personnel is a highly important consideration. If, as has been stated, a thermonuclear attack on the United States would involve millions of casualties and if the medical personnel itself will be decimated, it is obvious that there would not be enough duly qualified medical practitioners to meet this colossal task. It has long been recognized that there is an imperative need to develop and train all allied and paramedical personnel to assist physicians in the care of the injured in a major disaster.

This premise has been recognized and approved by the Office of Civil and Defense Mobilization and by leaders in medical civil defense, many of whom are participating in this conference. But, as yet, organized medicine has made no official statement to sanction or support such allied professional training.

This question has been raised by Major Gen. Silas B. Hays in the Sept. 20, 1958, issue of The Journal. In discussing the need for preparing paramedical workers he asks: "What is to be expected of these paramedical groups in a mass casualty situation? If the medical profession does not tell them, who is to? . . . These groups need guidance. Are they going to get it from the medical profession, or will they get it elsewhere? . . . I urge on American Medicine that this problem be faced forthwith and that a determination be made of the functions to be performed by the professions in emergencies which involve masses of casualties."

Although General Hays does not mention it in his article, I believe that the Medical Task Force on Personnel Training and Utilization, under the direction of Dr. Earle Standlee, is giving special consideration to paramedical training. They hope to define and to outline appropriate training programs for the various groups. This is most fortunate and may serve to dispel the uncertainties and misunderstandings that have existed in the past.

Of these professional allied medical workers in civil defense, I am here to represent the 90,000 dentists of the United States. For the past seven years, dentists have been placed in an equivocal position. They have been told that their basic medical training, their experience with handling patients in severe pain, and their cooperation with medicine in the care of their patients makes them high-priority professional personnel. This was shown in the recent wars when members of the dental corps

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Dental Consultant, Office of Civil and Defense Mobilization.

of the armed forces gave valuable assistance to the medical corps in the care of the wounded and often rendered meritorious casualty care when no medical men were available.

Training

Granting the potentiality of dentists for emergency casualty care, the fact still remains that the average dentist needs training in the initial treatment of various types of injuries. He may have some academic knowledge of what should be done, but he has had no actual experience in the handling of massive hemorrhage, extensive burns, fractures of long bones, or other serious bodily injuries. If, at a time of extreme emergency, the dentist is to be of any assistance to the physician, he must have had some orientation in these unfamiliar services. Perhaps, for dentists more than any of the paramedical group, there is need for additional training.

The OCDM, the American Dental Association, and leaders in medical civil defense have recommended training of dentists for emergency medical services. Accordingly, organized dentistry has done what it could to prepare itself, in spite of the anomalous situation in which it has been placed—that of training in medical services which they, by law, are not authorized to perform. More could have been accomplished if all dentists had been assured of the validity of such training and the medical profession had given more active cooperation in affording it.

Training of dentists has been of three types: (1) organized courses for key dental personnel; (2) establishment of courses in training in local dental societies in all parts of the United States; and (3) first-aid and casualty care instruction to students in dental schools. These have been largely instigated and promoted by the Health Office of OCDM, in full cooperation with the American Dental Association.

In 1953 and 1954, two courses were given for dentists at Olney, Md., and in 1955 a course was given for a combined dental and nursing group at Battle Creek, Mich. These were highly successful and produced many outstanding leaders in dental civil defense. In addition to these, many dentists have attended casualty care courses given at Walter Reed Army Hospital and at Brooke Medical Center by the Army. At the present time the number of dentists applying for these courses far exceeds the quotas of OCDM and the A. D. A.

In almost every state, courses of instruction have been given to members of local dental societies. In these, large numbers of dentists have actively and enthusiastically participated. As a rule, the instruction began with the standard Red Cross first-aid course. This was followed by lectures and demonstrations on the initial care of injuries by members of the medical profession. In some places, arrangements have been made for dentists to observe in the emergency receiving rooms of hospitals.

Although the dental schools have had no DEND Program, similar to MEND, over half of them on their own have included casualty care training as a part of their regular curriculum. This, as a rule, has been provided by the Red Cross and by the staffs of the associated medical schools.

Responsibilities

Organized dentistry is keenly interested in civil defense and is willing to assume any reasonable obligations assigned to it. Knowing full well that the usual dental services, in the immediate postattack period at least, will not be required, dentistry is willing to devote its skills and training to any disaster service for which they are qualified. As allied medical workers, they realize their need for training and orientation in methods of casualty care. The only way they can get it is through the active assistance and instruction of local medical men.

In many places physicians have cooperated with local dental societies and have carried out excellent courses of training. In others, physicians have been apathetic and unwilling to give the time and effort to training dentists. Very often, medical men are willing but are uncertain as to what should be taught and how the material should be presented. So, many dental societies have wished to have such training but have been limited solely to Red Cross first-aid instruction.

If organized medicine really believes that dentists should be prepared to act as paramedical assistants in a national disaster, it should be willing to prepare them for such services. This training can only come from medicine. If the medical profession does not assume it, it will not be done.

Two courses of action are indicated: First, the task force should define the scope of emergency casualty care functions dentists should be prepared to perform. This then should be approved and adopted by organized medicine. Second, members of the medical profession should be urged to cooperate in teaching dentists, on the local society level, the principles of initial casualty care. In this there is need for a syllabus to outline the instruction for each type of injury for the benefit of the medical instructors. The OCDM has proposed the setting-up of a "workshop" to draft such syllabuses when and if the scope of such training shall be defined.

Of course, in the long-range postattack and reconstruction period, dentists will perform their usual services on an emergency level. For this they need no training. But, if they are to be of any real benefit in the immediate postattack period, they need training now. This can only be afforded by the medical profession.

THE CIVIL DEFENSE ROLE OF NURSES

Catherine M. Sullivan, R.N., Battle Creek, Mich.

In discussing the civil defense role of nurses, I would like to describe what their role should be, in event of attack, and report some of the things being done about it. We believe the role of the nurse, in the event of an enemy attack, will be to adapt comprehensive nursing care to the situation where the numbers of patients needing care and treatment will greatly exceed the number of professional people available and where supplies, equipment, physical facilities, and utilities will be limited. In such a situation, the civil defense nursing service mission is to provide nursing care to the sick and injured and to prevent and minimize illness and injury of the surviving population. Thus, there are two major civil defense nursing service programs—medical care and public health.

Medical Care Planning and Facilities

Medical care planning includes that for both casualties and noncasualties. (Casualty is the term used for those who are sick or injured as a direct result of enemy action; noncasualty is the term used for those sick or injured but not as a direct result of enemy action.)

Casualty care includes care for burns, traumatic injuries, radiation sickness, illness resulting from biological and chemical warfare, and shock. In planning our nursing care, we must remember that the patients will be of all ages and that many of them may have multiple injuries and complicating medical conditions.

Plans for civil defense nursing are based on the following principles: 1. Self-help. Everyone should know how to care for himself or herself. 2. Neighbor help. Caring for family, friends, and neighbors includes knowing how to stop a hemorrhage, to maintain a free air passage, to perform artificial respiration, to splint fractures, to dress wounds, to handle the sick and injured properly, and to know principles of sanitation and cleanliness. 3. Priority of care. To function effectively as members of the medical team, nurses must know, understand, and accept the philosophy of priority of care: to give the best to the most with the least and by the fewest. In order to practice this, the sick and injured will be sorted into the following treatment categories: minimal, immediate, delayed, and expectant. 4. Regrading (now called expanded functions). Present thinking is that nurses will function within the realm of nursing, and many medical leaders feel that more lives will be saved by good nursing care than by up-graded functions. Nurses, however, will have to exercise more independent judgment and will be working with less direct medical supervision. 5. Total nursing care. The professional nurse will be responsible for total nursing care. This includes lifesaving techniques, measures to alleviate suffering, measures to prevent further injury, and supportive care.

The noncasualty group is the normal incidence of sickness and injury which is aggravated and increased due to the chaotic situation. It includes accidents, acute illness, chronic diseases, and communicable diseases.

Professional nurses will be on the staffs of the following facilities: 1. Emergency treatment station. This will provide first-aid care to minimal, essential lifesaving surgery to immediates, and a "holding" facility for delayed and expectant categories. 2. Civil defense emergency hospital. This will provide emergency medical and surgical care to the surviving population. 3. Existing hospitals. These will be expanded two, three, or more times. 4. Other. Nurses will be needed if large groups of the sick and injured are transported to other medical facilities or if "medical communities" are established.

I have given a brief summary of the nurse's role in the civil defense medical care plan. With that as a background, one can easily categorize nursing responsibilities into clinical, management, and teaching.

Nursing Responsibilities

It is our belief that if we survive the initial postattack period, the big problem will then be public health. This program will be responsible for the prevention, detection, and control of sickness and injury. It will include communicable disease control; prenatal and postnatal care; sanitation problems; contaminated food, milk, and water problems; and nutritional and emotional problems. Public health activities will function from established health departments and health centers. Reporting centers may be organized, and these, too, will require public health nursing service.

Professional nurses are prepared in many special fields of nursing, and this invites concern relative to assignment. It would be ideal if assignments could

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Nurse Consultant, Biophysical and Medical Sciences Office, Office of Civil and Defense Mobilization.

be made according to specialized preparation, and this should be done if possible. However, probable assignments will be made according to (1) where the nurses are, (2) what needs to be done, and (3) what they can do.

In any type of disaster, a nurse should know how to determine priorities; to evaluate patient's condition, personnel needs, and personnel and equipment available; to assign, supervise, and teach effectively; and last, but very important, to improvise. She should know her resources and plan solutions which include modifying care, modifying procedures without violating basic principles, modifying supplies and equipment, and the knowledge and ability to reallocate functions.

Civil defense is nonmilitary defense. It is everyone's business and is a way of life and will be for sometime to come. In civil defense, nurses have a dual responsibility—that of a citizen and that of a professional person. They first must be aware of this challenge, next, accept it, and then do something about it through training and education. The nursing profession has actively responded to the challenge of civil defense. Many civil defense training and educational programs have been conducted by the professional nursing organizations, the military, the American Red Cross, civil defense organizations, and schools of nursing.

In January, 1958, the National League for Nursing initiated a project to demonstrate ways of preparing nurses for mass casualty care and other nursing roles in civil defense. This is being done with an $80,000 contract with the Office of Civil and Defense Mobilization. The objective is to determine curriculum content needed for all types of nursing education programs, including in-service programs in hospitals. Demonstrations will be carried out in three colleges offering different types of nursing education programs and in one civilian hospital.

Massachusetts General Hospital will develop content in disaster nursing for diploma and in-service education programs. Skidmore College Department of Nursing will work on content for basic baccalaureate programs, and Teachers College, Columbia University, will work on content for advanced nursing education programs. Curriculum content for basic collegiate and practical nurse education programs will be developed at the University of Minnesota. The 18-month project is an initial step in preparing a plan for nursing education in national defense.

THE NUCLEI OF LEUKOCYTES.—For some years our attention has been directed to another form of individuality of human blood, namely the specific patterns identifiable in the highly complicated morphology of the nuclei of polymorphonuclear leukocytes. . . . In the early days of descriptive hematology, much attention was paid to the form of the nucleus, but the older literature is largely speculative. . . . The best available studies in this domain are those which enumerate the lobes of the nucleus. The Schilling count and the Arneth count are numerical expressions of the degree of nuclear segmentation. It is known that in the bone marrow the degree of segmentation is less than in the peripheral blood, and it is widely believed that the degree of segmentation is an index of maturity. It is also known that segmentation is increased in certain diseases and decreased in acute infections as well as in certain families, notably those having the gene for the Pelger-Huetanomaly. It has been shown however by Turpin, that the lobe count is a measurable aspect of individuality. Some individuals have an unusually high lobe count under physiologic conditions throughout life; others show a persistently low lobe count. Of great interest too is the entirely inexplicable finding, . . . that in mongolism the lobe count is lower than normal. The lobe count is at best a crude representation of the prevailing form of leukocyte and takes no account of the remarkable intricacy of the chromatin arrangement and the rich variety of appendages and projections from the lobes. That these features are modified by physiologic and pathologic circumstances including acute infections and such metabolic disorders as megaloblastic anemias is well recognized, but it is probably true that a given subject retains certain specific nuclear appearances throughout life. Heredity is probably important. Whether these characteristics are as specific as a patient's facial appearance or his fingerprints, whether they are such as would divide subjects into categories in the same way as the ABO blood groups or whether they merely give quantitative information should be determined.—D. K. Briggs, M.D., The Individuality of Nuclear Chromatin with Particular Reference to Polymorphonuclear Neutrophil Leukocytes, *Blood,* October, 1958.

THE JOURNAL
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DISASTER MEDICAL CARE

In this issue of The Journal are the papers presented at the Ninth County Medical Societies Civil Defense Conference held in Chicago on Nov. 8-9, 1958, and sponsored by the Council on National Defense of the American Medical Association. During the two-day conference, reports were presented on resuscitation techniques, shelter habitability, public health techniques for a nuclear age, reviews of three recent civil defense medical test programs, workshop sessions, and movies on selected subjects. This interesting program attracted representatives from 35 states and several foreign countries, and many important lessions were learned in the care of emergency medical services for large numbers of people.

Nearly every physician must ask himself the question how he would best function under conditions of disaster and what kind of medical care could he give. The threat of modern-day warfare with its capability of mass destruction of huge elements of our nation has imposed on the health professions a tremendous responsibility in the nation's efforts to survive. The saving of lives, particularly of those who can contribute to the survival effort, now assumes a new importance for the medical and allied professions.

A series of critical reviews of the types and the quality of medical care that was given after some disasters has not made pleasant reading. The sudden disruption of the normal well-ordered community life, a concomitant of all disasters, causes some profound changes in all aspects of life and seriously alters the environment in which medical care must be given. The variety of responses to meet these unpredictable events are conditioned by numerous factors. A small number of natural leaders emerge and give that steady and judicial leadership so vitally needed amid the chaotic surroundings. Experience and previous training are helpful and enable many to fall into routine patterns of action.

Physicians have been called on for exceptional and sustained effort after a disaster to assist the injured and the disturbed victims. Little training has been given in these fields of emergency medical care under traditional educational programs in the past, except the armed forces medical services. The ever-present threat of natural disaster has made physicians more aware of their obligation for this previously neglected field of medical care. Much has been learned from the experiences of industrial physicians, the armed forces medical services, and more recently civil defense medical organizations. The Council on National Defense, recognizing this trend, has recommended that its Committee on Civil Defense be renamed Committee on Disaster Medical Care, and the Board of Trustees has authorized the change. There has been an increasing number of papers published in The Journal and various specialty journals recommending sound scientific methods to be employed in emergency medical care.

The threat of nuclear attack and the ever-increasing improvement in weapon delivery systems have reduced the warning time and magnified the already complex and intricate problems of medical care in a thermonuclear age.

Eighteen months ago, the Federal Civil Defense Administration requested the American Medical Association to "recommend the planning, training and operational organization needed as a basis for a National Emergency Medical Care Plan for the treatment and care of casualties and noncasualties." The Commission created by the American Medical Association for this purpose, under the staff direction of Dr. Earle Standlee, is completing the final report to the Office of Civil and Defense Mobilization which will aid physicians in delineating their role in disaster medical care service. Developments in the field of civil defense have received renewed support and emphasis in recent months by the federal government, and the medical and health services are becoming more familiar with the detailed parts they are to play before, during, and after national emergencies.

The reports of this conference will enable physicians to give sound scientific medical care under conditions of austerity and disaster. Further study and observation will improve latent professional capabilities in providing any type of emergency medical care.

ORGANIZATION SECTION

NATIONAL CONFERENCE ON HOMEMAKER SERVICES

A National Conference on Homemaker Services, sponsored by the American Medical Association among 26 national, voluntary, and governmental agencies and organizations, will be held at the Edgewater Beach Hotel, Chicago, Feb. 10-11, 1959. Among the participants will be Dr. David B. Allman, member, Executive Committee of the Conference, Dr. Philip S. Barba, chairman, Finance Committee, and Dr. Lemuel C. McGee, chairman, Study Group on Industry and Labor and Homemaker Services. A number of other physicians and members of the Women's Auxiliaries will take part in the conference. Twelve study groups, which have held preconference discussions in the past few months, will prepare working papers for the meeting. These will serve as the bases for further discussion and for the formulation of plans to stimulate the development of such services and to strengthen the role of the voluntary agencies providing homemaker services throughout the country.

One significant development to be discussed will be of interest to all medical societies. It is the activity of the Passaic County, N. J., Homemaker Service which has been sponsored and supported by the local medical society of the state and which has demonstrated the effective role women's auxiliaries can assume in making homemaker services available to families in the community. Representation by all medical societies at the meeting is strongly recommended. Additional information regarding registration for the conference can be obtained by writing to the Council on Medical Service, American Medical Association, 535 N. Dearborn St., Chicago 10.

REPORT OF COMMISSION ON MEDICAL CARE PLANS

A limited supply of copies of Part 2 of the Report of the Commission on Medical Care Plans is available for distribution to physicians requesting single copies. This volume contains the "Statistical Appendices and Background Materials" to the commission's study. Requests for single copies should be addressed to Murray Klutch, Commission on Medical Care Plans, American Medical Association, 535 N. Dearborn St., Chicago 10. There will be no charge for single copies.

COUNCIL ON MEDICAL SERVICE

COMMITTEE ON MEDICAL AND RELATED FACILITIES

Study on Organizational and Professional Relationships Between Physicians in Private Practice and Those not in Private Practice.—The Committee on Medical and Related Facilities has undertaken a study of (1) the relationships of physicians in private practice to those not in private practice and (2) the growth and present status of public health services. At a recent planning conference it was decided that part one of the study should be concerned with the following physician groups not in the private practice of medicine: (1) physicians employed full time by official health agencies and other government services; (2) physicians employed full time by insurance companies, industries, pharmaceutical houses, voluntary health agencies, and research foundations; and (3) physicians employed full time in medical schools, hospitals, and other educational institutions.

More recently the Committee met with (group one) organizations representing full time public health physicians (i. e. American Public Health Association, Association of State and Territorial Health Officers, American Association of Public Health Physicians, and Public Health Service) to discuss relationships between these physicians and physicians in private practice. Part two of the study was also discussed and research methods evaluated.

A set of questions relating to the status of full time public health physicians in medical societies was sent to all county medical societies. The returns revealed that good relationships exist in most county medical societies. It is estimated that the study will take approximately one year during which time other conferences will be held and a number of national organizations visited by the staff.

MEDICAL NEWS

ALABAMA

Cancer Seminar in Birmingham.—The American Cancer Society, Alabama Division, Inc., will hold a Cancer Seminar Jan. 27-29, in Birmingham, in cooperation with the American College of Surgeons, Alabama Academy of General Practice, Jefferson County Dental Association, Jefferson County Medical Society, Medical Association of Alabama, and the Medical College of Alabama. Moderators for the three sessions will be Dr. Champ Lyons, Birmingham; Dr. John Day Peake, Mobile, president, American Cancer Society, Alabama Division, Inc.; and Dr. Joe Donald, Birmingham. Speakers and topics are as follows:

Cancer of the Breast, Dr. Alan Thal, Minneapolis.
Warts, Moles and Malignancy, Dr. George Andrews, New York City.
Cancer of the Head and Neck, Dr. Oliver Moore, New York City.
Radiation and Cancer, Dr. Milton Friedman, New York City.
Cancer of the Cervix, Dr. Herbert Schmitz, Chicago.
Chemotherapy of Cancer, Dr. Louis A. Leone, Richmond, Va.
Cancer of the Colon, Dr. Warren Cole, Chicago.
Cancer of the Prostate, Dr. W. W. Scott, Baltimore.
Cancer of the Lung, Dr. Thomas F. Nealon Jr., Philadelphia.

Question-and-answer periods will conclude each session. For information write Dr. Paul G. Reque, 601 Woodward Bldg., Birmingham 3, Ala., Program Chairman.

CALIFORNIA

Radiological Conference in Los Angeles.—The 11th annual Mid-Winter Radiological Conference, sponsored by the Los Angeles Radiological Society, will be held at the Statler Hotel, Los Angeles, Jan. 31-Feb. 1. Guest speakers will be: Dr. Peter Kerley, London, England; Prof. D. W. Smithers, London, England; Dr. F. N. Silverman, Cincinnati; and Dr. A. Finkelstein, Philadelphia. The conference fee of $20 includes two luncheon meetings featuring questions and answers. A banquet ($7.50 per plate) will be held Saturday evening, Jan. 31. For information and reservations, write Dr. Chester P. Bonoff, 1930 Wilshire Blvd., Los Angeles 57.

Dr. Mazia to Give Beattie Lecture.—Daniel Mazia, Ph.D. professor of zoology, University of California, Berkeley, will be guest speaker for the fifth annual Margaret Beattie Lecture presented by the Western Region of the American Association of Bioanalysts. He will address the Beattie dinner assembly Feb. 7 at the Clift Hotel, San Francisco, on "Biological Increase: The Life History of the Cell." The lecture series honors Prof. Margaret Beattie of the University of California School of Public Health "for her untiring efforts towards the elevation of standards and recruitment of clinical and public health laboratory personnel." The presentations are devoted to general subjects of pure science and are not restricted to methodology. Information on the dinner meeting may be obtained from William Reich, Walnut Creek–Lafayette Laboratories, 1409 Nursery Lane, Walnut Creek, Calif.

Annual Meeting in San Francisco.—The 88th annual session of the California Medical Association will be held Feb. 22-25 with headquarters at the Sheraton–Palace Hotel, San Francisco. Guest speakers will include Drs. Edwin B. Astwood, Boston; C. Rollins Hanlon, St. Louis; Donald L. McRae, Montreal, Quebec, Canada; and William Wallace Scott, Baltimore. Special guests of sections will be Drs. Warfield Garson, Chapel Hill, N. C., and Arthur Jones, Portland, Ore. The Cancer Commission of the California Medical Association will hold preconvention conferences Feb. 21, on which day five postgraduate courses will also be conducted. Dr. Francis E. West, president of the association, will open the general sessions Feb. 23 after which a symposium, "The Diagnosis and Management of Upper Gastrointestinal Bleeding," will be moderated by Dr. Edwin G. Clausen, Oakland. The second general meeting will be a tour of the Vallecitos Atomic Laboratory Feb. 24, with the president's dinner dance scheduled for that evening. A total of 14 symposiums and panel discussions will be presented. A motion-picture program is arranged for each day of the meeting. Scientific and technical exhibits and a ladies' program are arranged. For information write Mr. John Hunton, 450 Sutter St., San Francisco 8, Executive Secretary.

DISTRICT OF COLUMBIA

Nutrition Expert Dies.—Elmer M. Nelson, Ph.D., chief, Division of Nutrition, Food and Drug Administration, U. S. Department of Health, Education and Welfare, died suddenly at his home in Arlington, Va., Dec. 24. Dr. Nelson will be remembered for his contributions to the science of nutrition, his leadership in the regulatory labeling of nutritional products, and for his devoted service to the American Medical Association as a member of its Council

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Physicians are invited to send to this department items of news of general interest, for example, those relating to society activities, new hospitals, education, and public health. Programs should be received at least three weeks before the date of meeting.

on Drugs. He became affiliated with the staff of the Food and Drug Administration in 1935 and that same year also was elected to membership on the Council. Dr. Nelson served continuously as a member of the Council up to the time of his death, not only as an expert on vitamin preparations, but also as a member and later chairman of the Council's Committee on Nomenclature.

ILLINOIS

Chicago

Laboratory for Exfoliative Cytology.—Establishment of the Comdr. Eugene F. McDonald Jr. Memorial Laboratory for Exfoliative Cytology at the University of Chicago Medical Center has been announced by Dr. Lowell T. Coggeshall, dean of the university's Division of Biological Sciences, who said that formation of the laboratory has been financed by leaders in the radio and television industry as a memorial to the late founder-president of Zenith Radio Corporation of Chicago. Executives and business firms in the radio-television manufacturing industry have contributed about $155,000 and contributions are still being received by the university. The new laboratory includes a suite of five rooms located on the second floor of the Mothers' Aid Research Pavilion at the Chicago Lying-In Hospital on the University of Chicago campus. The laboratory is designed to make examinations for gynecological, lung, and other forms of cancer routine. The staff of cytologists is under the leadership of Dr. George L. Wied, assistant professor in the department of obstetrics and gynecology.

MASSACHUSETTS

Study of Fatal Highway Collisions.—The project "Research on Fatal Highway Collisions" already under way at the Harvard Medical School Department of Legal Medicine, Boston, has been awarded a grant of $809,000 by the U. S. Public Health Service for a five-year period. Other assistance in the form of laboratory service has been given by the Suffolk County Medical Examiner's office and the Chemistry Laboratory of the Massachusetts Department of Public Safety. Research on Fatal Highway Collisions will begin at the scene of the accident after alert by the State Police and the Registry of Motor Vehicles. The area studied will include metropolitan Boston and Cambridge to Route 128. Interviews at the scene, police station, hospital, and home will be carried out immediately. Weather and other environmental data will be taken. A traffic engineering analysis of the location will be made. Data on living drivers will include physical examination, history, vision, audition, psychological testing, psychiatric examination, social and family history, employment, vehicle and court records. Data will be integrated to (1) describe the conditions under which fatal highway collisions occur, (2) identify causes, (3) develop preventive measures, (4) aid in the interpretation of evidence, and (5) facilitate police training. The investigating team will include a psychologist, forensic pathologist, forensic psychiatrist, attorney, statistician, automotive engineer, social worker, ophthalmologist, traffic engineer, and physician. For information write Alfred L. Moseley, Department of Legal Medicine, Harvard Medical School, 25 Shattuck Street, Boston 15.

NEW JERSEY

Jefferson Medical Center Organizes Asthma Unit.—The Betty Bacharach Home, in association with the pediatric, medical, and psychiatric departments of the Jefferson Medical Center, has organized a unit for the treatment of intractable asthma in children. Children with perennial asthma of more than one year's duration and who are refractory to hyposensitization and other forms of medical treatment are eligible for admission. Absecon Island, on which the home is located, is relatively pollen-free. All facilities, including schools, are available within the institution. Children from 5 to 15 years will be considered for admission. The Betty Bacharach Home will underwrite the cost for all children admitted. For information write to Mr. Simon Lippman, Executive Secretary, Betty Bacharach Home, Atlantic City, N. J.

NEW YORK

Capt. Calvy Honored.—The Stitt Award of the Association of Military Surgeons of the United States was presented recently to Capt. George L. Calvy, MC, USN, chief of medicine at the U. S. Naval Hospital, St. Albans, for his clinical research with antibiotics in combating staphylococcic pneumonia. This award, consisting of a bronze plaque, an honorarium of $500, and a life membership in the association, is made annually by the Pfizer Laboratories Division, Charles Pfizer and Company, Inc., of Brooklyn "for meritorious work in the field of antibiotics."

Medical Seminar Cruise.—The New York University College of Medicine Alumni Association will sponsor a medical seminar cruise aboard the M.S. Italia visiting San Juan, St. Thomas, Ciudad Trujillo, Cap Haitien, and Nassau, sailing Feb. 21 (Alumni Day) and returning March 8. The faculty will include Drs. Claude E. Heaton, S. Bernard Wortis, John H. Mulholland Jr., Robert S. Hotchkiss, Clarence E. de la Chapelle, William Goldring, and Saul Krugman. The seminar constitutes 30 hours of category I credit for members of the American Academy of General Practice. For information write Dr. William N. Hubbard Jr., Associate Dean, New York University College of Medicine, Room 164, 550 First Ave., New York 16.

Annual Heart Conference.—"Heart in Industry" will be the theme of an all-day conference at the Waldorf-Astoria, New York City, Jan. 27, held under the auspices of the New York Heart Association. This is the fifth annual all-day conference sponsored by the association and the second on the industry theme. Dr. Norman Plummer, medical director, New York Telephone Company, is chairman of the planning committee. Former Governor Thomas E. Dewey will be the luncheon speaker. Dr. Jere W. Lord Jr., president of the association, will preside. With Dr. Edwin P. Maynard Jr., chief attending physician, the Brooklyn Hospital, presiding, speakers of the morning session will include Dr. Lawrence Hinkle Jr., Dr. Herman K. Hellerstein, Dr. S. Charles Franco, and Mr. Roland Baxt, executive director, Federation Employment and Guidance Service, New York City. Dr. Maynard will also act as moderator of the morning panel discussion. Dr. Irving S. Wright, past-president of the American and New York Heart associations, will preside at the afternoon workshop panel session which will consider questions related to the problem of heart diseases. For information write the New York Heart Association, 10 Columbus Circle, New York 19.

New York City

Conference on Hair Growth.—The New York Academy of Sciences, Section of Biological and Medical Sciences, will present a Conference on Hair Growth and Hair Regeneration Jan. 31, beginning at 9 a. m. Dr. Robert L. Kroc, chairman of the section, will open the meeting. Fourteen papers are scheduled for presentation, with the following two by Dr. George E. Rogers, Commonwealth Scientific and Industrial Research Organization, Wool Textile Research Laboratories, Victoria, Australia: "Recent Results on the Fine Structure of Hairs and Hair Follicles" and "Newer Findings on the Proteins and Enzymes of Hair Follicles." Attendance is limited to those invited to participate in these conferences and to interested members of the academy. For information write Dr. Irwin I. Lubowe, 667 Madison Ave., New York 21.

NORTH CAROLINA

Seminar on Occupational Health.—The University of North Carolina School of Medicine will sponsor the sixth annual Seminar on Occupational Health, to be held in Chapel Hill, Feb. 6. Other sponsors include the Occupational Health Committee of the Medical Society of the State of North Carolina and the Liberty Mutual Insurance Company. Special invitations will be sent to doctors in Virginia and South Carolina. Speakers for the program are Mr. R. E. Gordon, industrialist, Asheville; Dr. R. W. Borden, Goldsboro; Irene D. Courtenay, R. N., North Carolina State Board of Health; Dr. Joe M. Bosworth, Atlanta, Ga.; Dr. B. Dixon Holland, Secretary, Council on Industrial Health, A. M. A.; Dr. Elva Burgess, Charlotte; Dr. Eugene Van der Smissen, Division of Radiological Health, U. S. Public Health Service; and Dr. Thomas B. Barnett, associate professor of medicine, University of North Carolina School of Medicine.

PENNSYLVANIA

Plaques for Centenarians.—Sixty residents of the Commonwealth of Pennsylvania who reached their 100th birthday during 1958 were presented with testimonial plaques by The Medical Society of the State of Pennsylvania and the society wishes to find out who will be 100 in 1959. Since 1948, when the presentations were inaugurated, The Medical Society has provided hand-lettered, framed centenarian testimonials for 391 residents of the state. The testimonials have been presented either by officers of the county medical societies or the personal physician of the centenarian. The records show that 75% of Pennsylvanians who live to be 100 are women. A testimonial plaque will be presented to any resident of Pennsylvania who attains the age of 100 "in recognition of one whose life span exemplifies healthful living." Name and date of birth should be sent to The Medical Society of the State of Pennsylvania, 230 State St., Harrisburg.

Philadelphia

Fellowships in Gastroenterology Available.—There are available at the Jefferson Medical College and Hospital two additional fellowships for graduate training in gastroenterology, Dr. C. Wilmer Wirts, associate professor of medicine has announced. Stipend is $4,500 per year, and U. S. citizenship and a minimum of two years of medical residency are prerequisites. For information and application, write to Dr. Wirts, Jefferson Medical College of Philadelphia, 1025 Walnut St., Philadelphia 7.

British Lecturer.—Dr. Thomas Bedford, director of the Medical Research Council's Environmental Hygiene Research Unit, London, England, will deliver a paper at the opening session of the 65th annual meeting of the American Society of Heating and Air Conditioning Engineers in Philadelphia, Jan. 26-29, on "Researches on Heating and Ventilation in Relation to Human Comfort." Dr. Bedford, who also is a special lecturer in industrial hygiene, London School of Hygiene and Tropical Medicine, will participate in a topical session on comfort. After the meeting, he will proceed to lecture engagements at the Naval Air Development Center, Johnsville, Pa., the University of Pennsylvania, Philadelphia, the University of Minneapolis, the University of Illinois, Urbana, and the Harvard School of Public Health, Boston. Before returning to England, Dr. Bedford plans to visit Cleveland and Chicago.

TEXAS

International Assembly in San Antonio.—The 23rd annual meeting of the International Medical Assembly of Southwest Texas will be held Jan. 26-28 in the Gunter Hotel, San Antonio. A one-day seminar Jan. 25 will be presented by the San Antonio Division of the Post Graduate School of Medicine of the University of Texas. Each of the following speakers will give three presentations:

Drs. Frederic C. Bartter, Bethesda, Md.; Thomas L. Ball and Margaret H. D. Smith, New York City; Charles M. Norris and Harry E. Bacon, Philadelphia; John F. Holt, Ann Arbor, Mich.; E. Grey Dimond, Kansas City, Kan.; William Boyd, Toronto, Ont.; Charles G. Johnston, Detroit; Frank Foster and Cornelius E. Sedgwick, Boston; Milton L. McCall, New Orleans; William L. White, Pittsburgh; Col. Benjamin H. Sullivan Jr., Washington, D. C.; Merrill J. Reeh, Portland, Ore.; Franklin G. Ebaugh, Denver; and Rubin H. Flocks, Iowa City.

Technical displays, entertainment, and a ladies' program are arranged. Registration fee is $20. For information and registration, write the International Medical Assembly of Southwest Texas, 202 W. French Place, San Antonio 12, Texas.

WISCONSIN

Bowling Tournament.—The third annual showdown of physician "pinblasters" in Wisconsin and their wives is scheduled for Saturday, Feb. 7, in Madison. There will be mixed doubles, two classes of men's singles, men's doubles, a men's team event, and the ladies' singles championship. Serving as hosts and hostesses will be members of the Dane County Medical Society and its auxiliary. Defending champions, expected back to try again, include Drs. John B. Baldi, Milwaukee, and A. J. Schmidt, Sheboygan, men's singles; Drs. C. M. Carney and Erv T. Rechlitz, Beloit, men's doubles; and Mrs. J. W. Boren Jr., Marinette, auxiliary singles queen. Mixed doubles and the team match will be new events in 1959. A party will conclude the weekend of bowling. For information write the State Medical Society of Wisconsin, Box 1109, Madison 1, Wis.

GENERAL

Health Forum Meets in Chicago.—The 1959 National Health Forum, sponsored by the 64 agencies of the National Health Council, will be held March 17-19 at the Palmer House, Chicago, Dr. Norvin C. Kiefer, president of the council, has announced. Dr. James H. Sterner, medical director of Eastman Kodak Company, Rochester, N. Y., is chairman of the committee planning the meeting. The theme for the forum is "The Health of People Who Work." Dr. Arthur S. Flemming, secretary of the Department of Health, Education, and Welfare, Washington, D. C., will be a principal speaker. The three-day forum will mark the eighth year the council has sponsored cooperative sessions for discussion of major problems affecting the nation's health. The National Health Council inaugurated the National Health Forum in 1952 as a vehicle to direct public and professional attention to major problems in the field of health, of common interest to its member agencies. For information write the National Health Council, 1790 Broadway, New York 19.

Report on Easter Seal Activities.—According to the year-end report issued by the National Society for Crippled Children and Adults, a record total of 246,562 persons were served in programs and facilities operated by Easter Seal societies or in co-sponsored projects during 1958. The 38-year-old organization, operating in all 49 states, the District of Columbia, Hawaii, and Puerto Rico, likewise reports that there have been brought into existence some 50 new centers and programs including rehabilitation and treatment centers, camps, nursery schools, and new and expanded programs within already existing facilities, bringing total Easter Seal projects to more than 1,400. Services include care and treatment for those with orthopedic disorders, cerebral palsy, arthritis, poliomyelitis, muscular dystrophy, and multiple sclerosis. Through the Easter Seal Research Foundation, founded in 1956, a total of $376,578.28 in 49 grants has been made to 34 basic and clinical research projects in 29 universities and colleges. Last year a total of 56 resident camps were operated by the societies and an additional seven were co-sponsored. Dr. Dean W. Roberts is executive director of the National Society.

Trauma Surgeons Meeting in Colorado.—The Rocky Mountain Traumatic Surgical Society will meet at the Hotel Jerome, Aspen, Colo., Jan. 28-31. A one-hour panel discussion on "First Aid to Injured Skiers" will be held the afternoon of Jan. 29, with an organizational meeting held that morning. Physicians from Colorado will include the following: Drs. J. Sterling Baxter, Robert Barnard, and Charles S. Houston, Aspen; John Leidholdt, Col. Robert Anderson, Sid Blandford, Ralph Stuck, John Freed, William Stanek, Hugh MacMillian, William Coppinger, Charles Gaylord, William Gobe, and Robert Dean, Denver; and Robert Hall, Grand Junction. Papers by other participants are:

Injuries to the Spleen and Their Treatment, Dr. Donald Davenport, Long Beach, Calif.
Traumatic Knee Problems, Dr. A. C. Buergler, Akron, Ohio.
Fluophane Anesthesia in Spinal Fusion, Dr. Paul Evans, Los Angeles.

A summary panel will conclude the scientific session, and a business meeting and election of officers will conclude the meeting. For informaiton write Dr. Robert R. Odén, 420 Hyman St., Aspen, Colo.

Meeting of Surgeons in St. Louis.—A four-day sectional meeting of the American College of Surgeons will be held in St. Louis March 9-12, with headquarters at the Kiel Auditorium and with many sessions scheduled also in St. Louis hospitals. The program will include hospital clinics, panel discussions, symposiums, scientific papers, technical exhibits, medical motion pictures, and cine clinics in general surgery and in the specialties of thoracic surgery, urology, gynecology and obstetrics, ophthalmic surgery, and orthopedic surgery. Dr. Frank McDowell, St. Louis, associate clinical professor of surgery, Washington University School of Medicine, is chairman of the local advisory committee on arrangements for the scientific program. Hospital clinics have been arranged by staff representatives in leading St. Louis hospitals. Participating in the hospital clinics will be Barnes Hospital Group, Jewish Hospital, St. Louis City Hospital, St. Louis University Hospital, St. Luke's Hospital, and Veterans Administration Hospital. The joint nurses program, an annual feature of this meeting, will include discussions on comprehensive care of the patient who has successfully undergone pelvic evisceration, open technique in the management of burns, congenital heart disease, and other problems. Special films and tours and demonstrations at local hospitals are planned. Dr. H. Prather Saunders, associate director, American College of Surgeons, is in charge of the Sectional Meeting for the college.

Meeting on Clinical Research in California.—The 12th annual meeting of the Western Society for Clinical Research will be held Jan. 29-31 at the Golden Bough Theater, Carmel, Calif. The president's address will be given the afternoon of Jan. 29 by Dr. Herbert N. Hultgren, San Francisco. On Jan. 30, an alternate session will be held at the La Playa Hotel. Of the 48 papers scheduled for presentation, the following will be introduced by members:

The Estimation of Erythrocyte Survival Time in Hemolytic Disease from a Single Sample of Blood, Jean C. Sabine, Harry Lee, Catherine A. Lambert, and Myron Pollycove, San Francisco.
Metabolic Changes Produced by Human Growth Hormone (Li) in a Pituitary Dwarf, Roberto F. Escamilla, John J. Hutchings, William C. Deamer, and Choh Hao Li, San Francisco.
Effects of Bromsulfalein on the Cardio-portal Circulation Time, Ismael Mena, Leslie R. Bennett, R. Wilbur Melbye, Los Angeles.
Nature of Acute ST Changes in Experimental Coronary Occlusion, Werner E. Samson and Allen M. Scher, Seattle.
Effects of Clinical Digitalis Levels on Rubidium Uptake of Red Blood Cells, Jerold M. Lowenstein, William L. Caldwell, and Grover Liese, San Francisco.
Ventilatory Response of SCUBA Divers to CO_2 Inhalations, Herman F. Froeb, La Jolla, Calif.

The annual business meeting will be held at noon, Jan. 31. For information write Dr. William N. Valentine, University of California Medical Center, Department of Medicine, Los Angeles 24, Secretary-Treasurer.

CANADA

Physicians Meeting in Banff.—The American College of Physicians prairie regional meeting for Manitoba, Saskatchewan, and Alberta, will be held Jan. 29 at the Timberline Hotel, Banff, Alberta. The program will open with an address by Dr. F. A. L. Mathewson, governor of the college for Manitoba and Saskatchewan. Eleven papers are scheduled for presentation, including "Surgical Indications in Peptic Ulcer," by Dr. Fuller B. Bailey, Salt Lake City, Utah, regent of the college. At the evening dinner session, Dr. Bailey will be the speaker, discussing "The American College of Phyicians." A program for the ladies has been planned. Chairman of local arrangements is Dr. Stephen B. Thorson, 216 Medical Arts Building, Calgary, Alberta, Canada.

FOREIGN

Symposium on Bacterial Resistance to Antibiotics in Italy.—An International Symposium on "The Prevention of Bacterial Resistance to Antibiotics" will be held in Perugia, Italy, May 1-3, sponsored by the Italian Society of Obstetrics and Gynecology. The general topics of the sections will be (1) problems related to bacterial resistance to antibiotics today and (2) how to prevent bacterial resistance. Original reports, either clinical or in the basic sciences, will be considered, with definite priority given to the following:

Antibiotic resistant organisms in a maternity hospital.
Antibiotic resistant organisms as the cause of infection· obstetrical and gynecological departments.
Limitation of the use of antibiotics as prophylactic agents.
The newest antibiotic drugs; their use in emergency cases.

The official languages will be Italian and English. For information write: Segreteria del Simposio, Clinica Ostetrica e Ginecologia, Policlinico, Perugia, Italy.

Congress on Radiology in Munich.—The ninth International Congress for Radiology will be held in the Exposition Park, Munich, Germany, July 23-30, under the protectorate of the president of the republic, Prof. Dr. Theodor Heuss, and under the honorary presidency of Prof. Dr. H. Holthusen, of Hamburg, Prof. Dr. Boris Rayewsky, of Frankfurt, and general secretary Prof. Dr. H. v. Braunbehrens, of Munich. The new building of the German Roentgen Museum in Remscheid-Lennep will be dedicated in connection with this congress. The chief subjects of the scientific sessions will be: Intensification of Roentgen Pictures and Television in Roentgenological Diagnosis, Preoperative Irradiation of Malignant Tumors, Irradiation Exposure of the Population by the Medical Use of Irradiation, Automation and Automatic Diagnosis, Effect of Irradiation on the Metabolism and Cells, Chemical and Biological Protection Against Irradiation, and the Tasks of Radiology in the Present Era. Diagnostic and therapeutic problems, questions concerned with nuclear medicine and therapy, and laws regarding radiology will be discussed. The address of the secretary of the congress is: München 22, Reitmorstrasse 29, Germany.

CORRECTIONS

Addiction to Freely Obtainable Drugs.—In the Foreign Letter item from the United Kingdom entitled "Addiction to Freely Obtainable Drugs," in The Journal, Dec. 20 issue, page 2173, it is stated that a patient took 160 ml. of Chlorodyne "or one-third of an ounce." This should have read "or one-third of a pint."

Histoplasmosis.—In the editorial on histoplasmosis in the Dec. 27, 1958, issue of The Journal, page 2272, the statement "the causative fungus . . . is found in the feces of birds . . . bats, dogs, and various other mammals" was based on a popular misconception. Although the fungus is found in the soil where such animals are found and the infection in man often follows cleaning hen houses or pigeon lofts, repeated attempts to isolate the fungus from feces of any of these animals have been unsuccessful. The fungus may, however, be found in lesions of various autopsied birds and mammals.

EXAMINATIONS AND LICENSURE

NATIONAL BOARD OF MEDICAL EXAMINERS

National Board of Medical Examiners: Part II only, April 21-22; Parts I and II, June 16-17; Part I only, Sept. 9-10. Examinations must be received at least six weeks in advance of a specific examination date. Examining centers established after close of registration. Exec. Sec., Dr. John P. Hubbard, 133 South 36th St., Philadelphia 4.

EDUCATIONAL COUNCIL FOR FOREIGN MEDICAL GRADUATES, INC.

Educational Council for Foreign Medical Graduates, Inc.: Stations around the world, Feb. 17. Deadline for foreign applications was Nov. 17. The following examination will be held Sept. 22 with application deadline of June 22. Exec. Director, Dr. Dean F. Smiley, 1710 Orrington Ave., Evanston, Ill.

BOARDS OF MEDICAL EXAMINERS

Alabama: *Written*. Montgomery, June 16-18. Sec., Dr. D. G. Gill, State Office Bldg., Montgomery 4.

Alaska:* On application in Anchorage and Juneau. Sec., Dr. W. M. Whitehead, 172 South Franklin St., Juneau.

Arkansas:* *Examination and Reciprocity*. Little Rock, June 11-12. Sec., Dr. Joe Verser, Harrisburg.

Connecticut:* *Regular. Examination*. Hartford, March 10-12. Acting Sec., Dr. Louis P. Hastings, 160 St. Ronan St., New Haven.

Florida:* *Examination*. Miami Beach, June 22-24. Sec., Dr. Homer L. Pearson, 901 N.W. 17th St., Miami 36.

Georgia: *Examination and Reciprocity*. Atlanta, June. Sec., Mr. C. L. Clifton, 224 State Capitol, Atlanta 3.

Guam: *Subject to Call*. Act. Sec., Dr. F. L. Conklin, Agana.

Illinois: *Examination and Reciprocity*. Chicago, Jan. 26-30. Supt. of Registration, Mr. Fredric B. Selcke, Capitol Bldg., Springfield.

Maine: *Examination*. Portland, March 10-12. *Endorsement*. Portland, March 10. Sec., Dr. Adam P. Leighton, 142 High St., Portland.

Michigan:* *Examination*. Ann Arbor and Detroit, June 8-10. Sec., Dr. E. C. Swanson, 118 Stevens T. Mason Bldg., West Michigan Ave., Lansing 8.

Minnesota:* *Reciprocity*. St. Paul, February. Sec., Dr. F. H. Magney, 230 Lowry Medical Arts Bldg., St. Paul.

Montana: *Examination and Reciprocity*. Helena, April 7. Sec., Dr. Thomas L. Hawkins, 555 Fuller Ave., Helena.

Nebraska:* *Examination*. Omaha, June. Director, Mr. Husted K. Watson, Room 1009, State Capitol Bldg., Lincoln 9.

New Hampshire: *Examination and Endorsement*. Concord, Mar. 11-14. Sec., Dr. Edw. W. Colby, 61 So. State St., Concord.

New Mexico:* *Examination and Reciprocity*. Sante Fe, May 18-19. Sec., Dr. R. C. Derbyshire, 227 East Palace Ave., Santa Fe.

North Carolina: *Examination*. June Asst. Sec., Mrs. Louise J. McNeill, 716 Professional Bldg., Raleigh.

Oklahoma:* *Examination*. Oklahoma City, June 2-3. Exec. Sec., Mrs. E. L. Haidek, 813 Braniff Bldg., Oklahoma City.

Puerto Rico: *Examination and Reciprocity*. San Juan, March 3. Acting Secretary, Dr. Herminio Mendez Herrera, Box 9156, Santurce.

Texas:* *Examination and Reciprocity*. Fort Worth, June 22-24. Sec., Dr. M. H. Crabb, 1714 Medical Arts Bldg., Fort Worth 2.

Utah: *Examination*. Salt Lake City, July 8-10. Dir., Mr. Frank E. Lees, 324 State Capitol Bldg., Salt Lake City 1.

Vermont: *Examination and Reciprocity*. Burlington, Jan. 29-31. Sec., Dr. F. J. Lawliss, Richford.

Wyoming: *Examination and Reciprocity*. Cheyenne, Feb. 2. Sec., Dr. Franklin D. Yoder, State Office Bldg., Cheyenne.

BOARDS OF EXAMINERS IN THE BASIC SCIENCES

Arkansas: *Examination*. Little Rock, May 4-5. Sec., Dr. S. C. Dellinger, University of Arkansas, Fayetteville.

Connecticut: *Examination*. New Haven, Feb. 14. Exec. Asst., Mrs. Regina G. Brown, 258 Bradley St., New Haven 10.

Florida: *Examination*. Miami, June 6. Sec., Mr. M. W. Emmel, University of Florida, Box 340, Gainesville.

Kansas: *Examination*. Kansas City, June. Sec., Dr. L. C. Heckert, Pittsburg.

Michigan: *Examination*. Ann Arbor and Detroit, Feb. 12-13. Sec., Mrs. Anne Baker, 116 Stevens T. Mason Bldg., West Michigan Ave., Lansing.

Oklahoma: *Examination*. Oklahoma City, Mar. 27-28. Exec. Sec., Mrs. L. Haidek, 813 Braniff Bldg., Oklahoma City.

Rhode Island: *Examination*. Providence, Feb. 18. Administrator of Professional Regulation, Mr. Thomas B. Casey, 366 State Office Bldg., Providence.

Texas: *Examination*. April 1959. Certificates issued by reciprocity and waiver on the first and fifteenth of each month. Sec., Bro. Raphael Wilson, 407 Perry-Brooks Bldg., Austin.

Wisconsin: *Examination*. Madison, April 4. Final date for filing application is March 27. Milwaukee, June 6. Final date for final application is May 29. Sec., Mr. W. H. Barber, 621 Ransom St., Ripon.

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*Basic Science Certificate required.

College; formerly on the faculty of Harvard Medical School in Boston; served as a battalion surgeon in the 96th quartermaster battalion in Europe during World War II; from 1953 to 1956 chief of the section of clinical neurophysiology at the National Institute of Neurological Diseases and Blindness in Bethesda, Md.; on the staff of Jefferson Hospital; died in St. Luke's and Children's Medical Center Nov. 18, aged 41.

Colef, Irving Edwin, Corpus Christi, Texas; Detroit College of Medicine and Surgery, 1930; member of the Industrial Medical Association; interned at the Butterworth Hospital in Grand Rapids, Mich.; formerly practiced in Benton Harbor, Mich., where he was associated with the Mercy Hospital; died Nov. 4, aged 55.

Cumbler, George William Ⓢ New York City; University and Bellevue Hospital Medical College, New York City, 1920; specialist certified by the American Board of Internal Medicine; member of the American Rheumatism Association; fellow of the American College of Physicians; served as visiting physician, New York City Correction Hospitals, attending physician, Grasslands Hospital in Valhalla, N. Y., and St. Agnes Hospital in White Plains, N. Y., where he was chief of the arthritis clinic; chief of arthritis clinic, White Plains, (N. Y.) Hospital; died Nov. 14, aged 65.

Cusick, Laurence Francis Ⓢ Nahant, Mass.; Harvard Medical School, Boston, 1904; medical examiner in the Lynn district for 21 years; on the staffs of the Union Hospital and the Lynn Hospital, in Lynn, where he died Nov. 3, aged 79.

Davey, Byron Theodore, New York City; University of Toronto Faculty of Medicine, Toronto, Ontario, Canada, 1905; an associate member of the American Medical Association; on the staff of the Midtown Hospital, where he died Nov. 6, aged 82.

Der Brucke, Maurice G., Brooklyn; Long Island College Hospital, Brooklyn, 1920; specialist certified by the American Board of Obstetrics and Gynecology; fellow of the International College of Surgeons and the American College of Surgeons; associated with the Brooklyn Doctors Hospital, Coney Island Hospital, and the Caledonian Hospital, where he died Nov. 15, aged 60.

Dewis, Edwin Grafing Ⓢ Asbury Park, N. J.; born in New York City in 1892; New York Homeopathic Medical College and Flower Hospital, New York City, 1918; member of the Industrial Medical Association and the American Public Health Association; veteran of World War I; served as president and secretary of the Association of Life Insurance Medical Directors, as secretary and treasurer of the Society for the Prevention of Asphyxiation Deaths, and vice-president of the International Congress on Life Assurance Medicine and a member of its permanent international committee; for many years chief medical director of the Prudential Insurance Company of America, which he joined in 1920; died Nov. 9, aged 66.

Eaton, Lealdes McKendree Ⓢ Rochester, Minn.; born in Owaneco, Ill., Feb. 3, 1905; Rush Medical College, Chicago, 1932; interned at the Cook County Hospital in Chicago; in 1933 became a fellow in neurology in the Mayo Foundation and in 1936 a consultant in neurology on the staff of the Mayo Clinic, where he was chairman of the sections of neurology and professor of neurology; specialist certified by the American Board of Psychiatry and Neurology, of which he was a director and examiner; president of the Association for Research in Nervous and Mental Diseases; in 1953 president and formerly secretary of the Central Neuropsychiatric Association; member of the American Neurological Association, the Alpha Omega Alpha honorary medical society, and the Nu Sigma Nu; fellow of the American Academy of Neurology; in 1956 chairman of the Section on Nervous and Mental Diseases of the American Medical Association; member of the advisory board of the Myasthenia Gravis Foundation; author and coauthor of more than 50 papers on various neurologic problems; editor of the book, "Clinical Examinations in Neurology," written by members of the sections of neurology and published in 1956; died in the Methodist–Worrall Hospital Nov. 18, aged 53.

Emerson, George Short Ⓢ Fitzwilliam, N. H.; Baltimore Medical College, 1897; served many years on the school board and the Fitzwilliam new school was named for him; a member of the board of health for many years; a member of the staff of the Elliot Community Hospital in Keene; died Nov. 7, aged 87.

Epstein, Harry Benjamin, Newark, N. J.; born in Elizabeth, June 20, 1872; New York University Medical College, New York City, 1896; also a graduate in pharmacy; an associate member of the American Medical Association; fellow of the American College of Surgeons; past-president of the Anatomical and Pathological Society of Northern New Jersey and the Academy of Medicine of Northern New Jersey, of which he was a trustee; an honorary member of the Society of Surgeons of New Jersey; veteran of World War I; associated with the Presbyterian, Newark City, and Newark Beth Israel hospitals; served as medical director of the Jewish Children's Home; author of "William Shakespeare, M.D."; died at his home in East Orange Nov. 22, aged 86.

Herron, Stanford Morton, Jackson, Tenn.; University of Tennessee College of Medicine, Memphis, 1919; member of the Tennessee State Medical As-

College; formerly on the faculty of Harvard Medical School in Boston; served as a battalion surgeon in the 96th quartermaster battalion in Europe during World War II; from 1953 to 1956 chief of the section of clinical neurophysiology at the National Institute of Neurological Diseases and Blindness in Bethesda, Md.; on the staff of Jefferson Hospital; died in St. Luke's and Children's Medical Center Nov. 18, aged 41.

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College; formerly on the faculty of Harvard Medical School in Boston; served as a battalion surgeon in the 96th quartermaster battalion in Europe during World War II; from 1953 to 1956 chief of the section of clinical neurophysiology at the National Institute of Neurological Diseases and Blindness in Bethesda, Md.; on the staff of Jefferson Hospital; died in St. Luke's and Children's Medical Center Nov. 18, aged 41.

Colef, Irving Edwin, Corpus Christi, Texas; Detroit College of Medicine and Surgery, 1930; member of the Industrial Medical Association; interned at the Butterworth Hospital in Grand Rapids, Mich.; formerly practiced in Benton Harbor, Mich., where he was associated with the Mercy Hospital; died Nov. 4, aged 55.

Cumbler, George William Ⓜ New York City; University and Bellevue Hospital Medical College, New York City, 1920; specialist certified by the American Board of Internal Medicine; member of the American Rheumatism Association; fellow of the American College of Physicians; served as visiting physician, New York City Correction Hospitals, attending physician, Grasslands Hospital in Valhalla, N. Y., and St. Agnes Hospital in White Plains, N. Y., where he was chief of the arthritis clinic; chief of arthritis clinic, White Plains, (N. Y.) Hospital; died Nov. 14, aged 65.

Cusick, Laurence Francis Ⓜ Nahant, Mass.; Harvard Medical School, Boston, 1904; medical examiner in the Lynn district for 21 years; on the staffs of the Union Hospital and the Lynn Hospital, in Lynn, where he died Nov. 3, aged 79.

Davey, Byron Theodore, New York City; University of Toronto Faculty of Medicine, Toronto, Ontario, Canada, 1905; an associate member of the American Medical Association; on the staff of the Midtown Hospital, where he died Nov. 6, aged 82.

Der Brucke, Maurice G., Brooklyn; Long Island College Hospital, Brooklyn, 1920; specialist certified by the American Board of Obstetrics and Gynecology; fellow of the International College of Surgeons and the American College of Surgeons; associated with the Brooklyn Doctors Hospital, Coney Island Hospital, and the Caledonian Hospital, where he died Nov. 15, aged 60.

Dewis, Edwin Grafing Ⓜ Asbury Park, N. J.; born in New York City in 1892; New York Homeopathic Medical College and Flower Hospital, New York City, 1918; member of the Industrial Medical Association and the American Public Health Association; veteran of World War I; served as president and secretary of the Association of Life Insurance Medical Directors, as secretary and treasurer of the Society for the Prevention of Asphyxiation Deaths, and vice-president of the International Congress on Life Assurance Medicine and a member of its permanent international committee; for many years chief medical director of the Prudential Insurance Company of America, which he joined in 1920; died Nov. 9, aged 66.

Eaton, Lealdes McKendree Ⓜ Rochester, Minn.; born in Owaneco, Ill., Feb. 3, 1905; Rush Medical College, Chicago, 1932; interned at the Cook County Hospital in Chicago; in 1933 became a fellow in neurology in the Mayo Foundation and in 1936 a consultant in neurology on the staff of the Mayo Clinic, where he was chairman of the sections of neurology and professor of neurology; specialist certified by the American Board of Psychiatry and Neurology, of which he was a director and examiner; president of the Association for Research in Nervous and Mental Diseases; in 1953 president and formerly secretary of the Central Neuropsychiatric Association; member of the American Neurological Association, the Alpha Omega Alpha honorary medical society, and the Nu Sigma Nu; fellow of the American Academy of Neurology; in 1956 chairman of the Section on Nervous and Mental Diseases of the American Medical Association; member of the advisory board of the Myasthenia Gravis Foundation; author and coauthor of more than 50 papers on various neurologic problems; editor of the book, "Clinical Examinations in Neurology," written by members of the sections of neurology and published in 1956; died in the Methodist–Worrall Hospital Nov. 18, aged 53.

Emerson, George Short Ⓜ Fitzwilliam, N. H.; Baltimore Medical College, 1897; served many years on the school board and the Fitzwilliam new school was named for him; a member of the board of health for many years; a member of the staff of the Elliot Community Hospital in Keene; died Nov. 7, aged 87.

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Herron, Stanford Morton, Jackson, Tenn.; University of Tennessee College of Medicine, Memphis, 1919; member of the Tennessee State Medical As-

DEATHS

Arthur, William John, Merriam, Kan.; University of Kansas School of Medicine, Kansas City, Kan., 1953; interned at the Memorial Hospital in South Bend, Ind.; served a residency at the University of Kansas Medical Center in Kansas City, Kan., and the Veterans Administration Hospital in Kansas City, Mo.; died Nov. 16, aged 39.

Bassett, Henry Linn, Yardley, Pa.; Jefferson Medical College of Philadelphia, 1901; an associate member of the American Medical Association; in 1953 was cited by the Bucks County Medical Society for 50 years of service; for many years on the staff of the Mercer Hospital in Trenton, N. J., where he died Nov. 29, aged 84.

Berg, Nathaniel Ⓜ Long Island City, N. Y.; L. R. C. P., Edinburgh, L. R. C. S., Edinburgh, and L. R. F. P. & S., Glasgow, Scotland, 1937; veteran of World War II; died Nov. 26, aged 47.

Bernheim, Bertram Moses, Baltimore; born in Paducah, Ky., Feb. 15, 1880; Johns Hopkins University School of Medicine, Baltimore, 1905; associate professor emeritus of surgery at his alma mater; an associate member of the American Medical Association; member of the founders group of the American Board of Surgery; a founder of the American College of Surgeons; during World War I served overseas with Johns Hopkins Base Unit, captain and later major in the medical corps of the U. S. Army, American Expeditionary Force; received a citation for his work with combat troops during the fighting around Chateau Thierry in the summer of 1918; served on the staffs of the Johns Hopkins, Union Memorial, and West Baltimore General hospitals, the Hospital for Women of Maryland, and the Church Home and Infirmary; the Norton Medical Award for 1947 was given to him for his book "A Surgeon's Domain"; the award was made for the best book by a professional man written for the layman; author of "Surgery of the Vascular System," published in 1913, "Blood Transfusion, Hemorrhage and the Anemias," 1917, "Passed as Censored," 1918, "Medicine at the Crossroads," 1939, "Adventure in Blood Transfusion," 1942, and "The Story of the Johns Hopkins," 1948; died in the Union Memorial Hospital Nov. 28, aged 78.

Bilek, George James Ⓜ Chicago; Indiana University School of Medicine, Indianapolis, 1929; on the staff of the Evangelical Hospital; served during World War II; died Nov. 28, aged 55.

Bisson, Napoleon Ⓜ Waterville, Maine; Baltimore Medical College, 1907; fellow of the American College of Surgeons; veteran of World War I; during World War II medical examiner for Kennebec County and the examining physician for Waterville area Selective Service draft board; member of the staffs of Sisters' and Thayer hospitals; a director of the Federal Trust Company; Knight of St. Gregory of the Roman Catholic Church; died Nov. 5, aged 76.

Boettcher, Heinz Hans Otto, Terrell, Texas; Universitat Leipzig Medizinische Fakultat, Saxony, Germany, 1937; resident on the staff of the Terrell State Hospital; died near Ludlow, Okla., Nov. 8, aged 45.

Bondoc, Jose Ma, Richmond, Ind.; University of Santo Tomas Faculty of Medicine and Surgery, Manila, P. I., 1943; interned at the Quincy City (Mass.) Hospital; resident surgeon at the Richmond State Hospital; died in the Reid Memorial Hospital Nov. 3, aged 40.

Budlong, Lewis Stanley, Watertown, N. Y.; University and Bellevue Hospital Medical College, New York City, 1899; an associate member of the American Medical Association; on the staffs of the House of the Good Samaritan and Mercy hospital; died in the Jefferson County Sanatorium and Hospital for Chronic Diseases Nov. 2, aged 80.

Bush, David Hardman, Mount Sterling, Ky.; University of Louisville (Ky.) Medical Department, 1898; an associate member of the American Medical Association; served as state senator; on the staff of Mary Chiles Hospital; died Nov. 7, aged 86.

Butzin, Theodore Arzt, Beverly Hills, Calif.; University of Minnesota Medical School, Minneapolis, 1928; died Nov. 14, aged 63.

Carter, John William, Syracuse, N. Y.; Syracuse University College of Medicine, 1927; interned at the Crouse-Irving Hospital in Syracuse, and St. Michael's Hospital in Newark, N. J.; veteran of World War I; alderman in the Sixth Ward for two terms; on the staffs of St. Joseph's and Onondaga General hospitals; a physician for the New York State Athletic Commission many years; died Nov. 11, aged 59.

Chatfield, Paul Oakes, Philadelphia; Johns Hopkins University School of Medicine, Baltimore, 1943; interned at Johns Hopkins Hospital in Baltimore; assistant professor of neurology at Jefferson Medical

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Ⓜ Indicates Member of the American Medical Association.

College; formerly on the faculty of Harvard Medical School in Boston; served as a battalion surgeon in the 96th quartermaster battalion in Europe during World War II; from 1953 to 1956 chief of the section of clinical neurophysiology at the National Institute of Neurological Diseases and Blindness in Bethesda, Md.; on the staff of Jefferson Hospital; died in St. Luke's and Children's Medical Center Nov. 18, aged 41.

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Herron, Stanford Morton, Jackson, Tenn.; University of Tennessee College of Medicine, Memphis, 1919; member of the Tennessee State Medical As-

sociation; secretary of the Madison County Tuberculosis Association and the Consolidated Medical Assembly of West Tennessee; past-president and secretary of the Tennessee Tuberculosis Association and for many years a member of the board; twice served as president of Jackson Rotary and was past Rotary District governor; on the staffs of the Jackson–Madison County General Hospital and the Webb–Williamson Hospital, where he died Oct. 22, aged 67.

Scott, Edgar Leonard, Chattanooga, Tenn.; Meharry Medical College, Nashville, 1932; on the staff of the Carver Memorial Hospital, where he died Oct. 21, aged 52.

Johnston, Frank, Milton, Ill.; Missouri Medical College, St. Louis, 1897; member of the staff of Illini Hospital in Pittsfield; died in Winston–Salem, N. C., Oct. 23, aged 85.

Julius, Abraham J., New York City; Long Island College Hospital, Brooklyn, 1922; died in the Veterans Administration Hospital Oct. 14, aged 59.

Kearney, Elmer Frank Ⓜ Oregon, Mo.; Barnes Medical College, St. Louis, 1906; past-president of the school board; veteran of World War I; served as probate judge and then magistrate judge in Holt County since 1939; died in the Veterans Administration Center, Wadsworth, Kan., Oct. 22, aged 78.

King, Wessie Price, Weston, W. Va.; University of Maryland School of Medicine, Baltimore, 1891; an associate member of the American Medical Association; for many years physician and surgeon for the Baltimore and Ohio Railroad; on the staff of the Weston City Hospital; died Nov. 8, aged 88.

Koch, George William Ⓜ Anaheim, Calif.; Rush Medical College, Chicago, 1904; for many years practiced in Sioux City, Ia.; served on the staff of St. Joseph Hospital in Orange; died in the Anaheim Memorial Hospital Oct. 22, aged 79.

Kotanchik, Walter Edward Ⓜ Shamokin, Pa.; Jefferson Medical College of Philadelphia, 1933; interned at the Williamsport (Pa.) Hospital; served a residency at the Brooklyn Eye and Ear Hospital; veteran of World War II; died in the Geisinger Memorial Hospital, Danville, Oct. 23, aged 55.

Lamb, William Paul, East Orange, N. J.; University and Bellevue Hospital Medical College, New York City, 1904; for many years assistant medical director of the Prudential Insurance Company; died Nov. 6, aged 78.

Lawton, William Henry Ⓜ Colonel, U. S. Air Force, retired, Fort Pierce, Fla.; born in Garnett, S. C., Nov. 19, 1897; George Washington University School of Medicine, Washington, D. C., 1927; service member of the American Medical Association; member of the Aero Medical Association; specialist certified by the American Board of Preventive Medicine; served in the U. S. Army from 1928 to 1949, when he transferred to the U. S. Air Force; was awarded the Legion of Merit; in November, 1958, was awarded the McLester Award by the Association of Military Surgeons of the United States for work in nutrition; died in the USAF Hospital, Palm Beach Air Force Base, Nov. 6, aged 60.

Longbrake, Pearl Duette Ⓜ Marysville, Ohio; Ohio Medical University, Columbus, 1897; died in the Memorial Hospital Oct. 24, aged 83.

McCarthy, John Anthony Ⓜ Braintree, Mass.; Tufts College Medical School, Boston, 1930; service member of the American Medical Association; member of the American College of Chest Physicians; veteran of World War I; formerly associated with the Veterans Administration in Boston; died in the Quincy City (Mass.) Hospital Oct. 28, aged 61.

McDougal, Clyde Cameron, Westport, Conn.; University of Buffalo School of Medicine, 1932; served on the faculty of New York Medical College, Flower and Fifth Avenue Hospitals in New York City, where he formerly practiced and where he was associated with Morrisania and Columbus hospitals; died in the Veterans Administration Hospital, New York City, Oct. 9, aged 63.

Marcus, Isaac Horatio, Brooklyn; University and Bellevue Hospital Medical College, New York City, 1908; served on the staff of the Unity Hospital; died in the Long Island College Hospital Oct. 11, aged 73.

Martin, Aaron Wise Ⓜ Hillsville, Va.; George Washington University School of Medicine, Washington, D. C., 1912; died Aug. 30, aged 79.

Mendel, Max Louis, Vicksburg, Miss.; Rush Medical College, Chicago, 1907; veteran of World War I; for many years practiced in Chicago, where he was on the staffs of the Englewood and Illinois Central hospitals and head of the medical department of the Chesapeake and Ohio Railroad; charter member of the University of Chicago Phi Gamma Delta fraternity and was a member of Nu Sigma Nu medical fraternity; member of the Illinois State Medical Society; died Oct. 18, aged 76.

Meyer, Selma E., Kew Gardens, N. Y.; Friedrich–Wilhelms–Universität Medizinische Fakultät, Berlin, Prussia, 1917; died Oct. 14, aged 77.

Michael, Guy H., Parsons, W. Va.; born Jan. 1, 1896; St. Louis College of Physicians and Surgeons, 1922; past-president and secretary of the Barbour–Randolph–Tucker Counties Medical Society; an associate member of the American Medical Association; honorary life member, served as a member of the council, and past-vice-president of the West Virginia State Medical Association; veteran of World War I; served as mayor of Belington; for six years a member of the Tucker County Board of Education; formerly county health officer; a charter member of the Parsons Lions Club; superintendent of the Tucker County Hospital; died Nov. 2, aged 62.

Mock, Lewis Emmett, Mountain City, Tenn.; University of Tennessee Medical Department, Nashville, 1906; died Sept. 10, aged 83.

Moore, Darius Carrier, Beaver, Pa.; Jefferson Medical College, Philadelphia, 1903; an associate member of the American Medical Association; served as a member and president of the board of directors of Monaca (Pa.) First National Bank; died Oct. 29, aged 79.

Moore, Wallace P. Ⓜ Memphis, Tenn.; Memphis Hospital Medical College, 1902; served as city and county health officer, and county jail physician; died Nov. 2, aged 77.

Myers, Lotta Wright, New York City; Woman's Medical College of the New York Infirmary for Women and Children, New York City, 1897; an associate member of the American Medical Association; died in the Roosevelt Hospital Oct. 5, aged 90.

Perkins, Edward Carter Ⓜ Hartford, Conn.; Columbia University College of Physicians and Surgeons, New York City, 1910; for many years a medical missionary in China; died in the Mitchell Convalescent Hospital, West Hartford, Oct. 30, aged 82.

Perry, Robert Jackson Ⓜ Springville, Tenn.; University of the South Medical Department, Sewanee, 1905; died Nov. 1, aged 90.

Raphael, Joseph, Brooklyn; Long Island College Hospital, Brooklyn, 1904; formerly on the faculty of his alma mater; an associate member of the American Medical Association; fellow of the American College of Surgeons; served as secretary of the Medical Society of the County of Kings as well as member of the board of trustees and former chairman of the Workmen's Compensation Commission; veteran of World War I; consulting surgeon at Kings County, Caledonian, and Jewish hospitals; died in the Brooklyn Hospital Oct. 11, aged 80.

Richards, John Harold Ⓜ New York City; Cornell University Medical College, New York City, 1905; formerly on the faculty of his alma mater and the New York Polyclinic Medical School and Hospital; served on the staffs of Bellevue and New York hospitals; died in the Westchester division of the New York Hospital in White Plains Oct. 27, aged 78.

Sawyer, Earle Dewey Ⓜ Wenatchee, Wash.; Tufts College Medical School, Boston, 1907; died Oct. 24, aged 74.

Schmidhofer, Max Ⓜ Chicago; Jenner Medical College, Chicago, 1913; medical examiner at 5th Army headquarters; died in the Illinois Masonic Hospital Nov. 11, aged 74.

Schmitt, Alton Joseph Ⓜ Sheboygan, Wis.; University of Wisconsin Medical School, Madison, 1931; served an internship at the Long Island College Hospital in Brooklyn, where he served a residency; died in Chicago Nov. 7, aged 54.

Schultz, J. Albert Ⓜ Albert Lea, Minn.; Rush Medical College, Chicago, 1902; died in the Naeve Hospital Oct. 31, aged 81.

Scott, Ernest Winfield, Ormond Beach, Fla.; University of Virginia Department of Medicine, Charlottesville, 1907; formerly associated with the U. S. Public Health Service; served as assistant medical director of the Equitable Life Insurance Company; died Sept. 30, aged 73.

Smith, Morris, New York City; Long Island College Hospital, Brooklyn, 1913; an associate member of the American Medical Association; died Sept. 28, aged 75.

Stutsman, Carl, Burlington, Iowa; Northwestern University Medical School, Chicago, 1893; served as city health officer; on the staffs of the Burlington and Mercy hospitals; died Oct. 27, aged 90.

Thom, James Alexander, Baton Rouge, La.; Medical Department of Tulane University of Louisiana, New Orleans, 1912; member of the Louisiana State Medical Society; on the staff of the Baton Rouge General Hospital, where he died Oct. 30, aged 76.

Younkin, J. Noble, Chesterfield, Ind.; American Medical College, St. Louis, 1901; veteran of World War I; died Oct. 26, aged 83.

Viktoryn, John Wenceslaus, Cleveland; Western Reserve University School of Medicine, Cleveland, 1932; veteran of World War II; on the staff of St. Alexis Hospital, where he served an internship and residency; died Oct. 22, aged 53.

Weber, Henry Charles Ⓜ Captain, U. S. Navy, retired, Drexel Hill, Pa.; Marquette University School of Medicine, Milwaukee, 1914; entered the U. S. Navy June 29, 1921; retired March 1, 1947; specialist certified by the American Board of Ophthalmology and the American Board of Otolaryngology; member of the American Academy of Ophthalmology and Otolaryngology; fellow of the American College of Surgeons; served on the staff of the Halifax District Hospital in Daytona Beach, Fla.; died in the U. S. Naval Hospital, Bethesda, Md., Oct. 30, aged 71.

FOREIGN LETTERS

BRAZIL

Biopsy of the Endometrium.—Dr. N. M. Fonseca (*Anais brasileiros de ginecologia,* vol. 46, 1958) studied endometrial biopsy specimens of 500 currettements to ascertain whether the results of the biopsy could be used as a test of ovarian function. This use is based on the demonstration by Hitschmann and Adler of the cyclic modifications of the endometrium and on the evidence accumulated by Schroeder of the correlation between the ovarian and the endometrial cycles. This study permitted a tentative classification of the alterations under the following headings: (1) simple diffuse hyperplasia, 200 cases; (2) cystic diffuse hyperplasia, 80; (3) hyperplasia of the glands, 63; (4) hyperplasia of the stroma, 5; (5) circumscribed hyperplasia, 15; (6) mixed endometrium, 53; (7) hyperplastic mixed endometrium, 33; and (8) posthyperplastic secretory endometrium, 23. The late proliferative, the persistent secretory, and the atrophic types of endometrium were not included in this series. These types of endometrium can only be diagnosed on the basis of clinical data not always available to the pathologist.

The author concluded that biopsy of the endometrium should be performed, as far as possible, at the end of the menstrual cycle. The existence of a secretory endometrium at the end of the cycle, in a eumenorrheic patient, signifies, in nearly all cases, that there was ovulation and that the ovary functioned normally during the cycle. The existence of a physiopathological endometrium strongly suggests a functional disturbance of the ovary. The single biopsy of the endometrium, as with other functional tests of the ovary, is not sufficient for the determination of ovarian function. In order to assess the functional state of the ovary, it is necessary to take an endometrial biopsy specimen together with other functional tests of the ovary. The accuracy of the functional evaluation will increase with the number of tests used. The cases with hyperplasia represented 62.5% of the total, if the persistent secretory, the late proliferative, and the atrophic types of endometrium were excluded.

Cardiovascular Syphilis.—Dr. M. de Brito Avila and co-workers presented to the Associação Paulista de Medicina a report of 196 patients with cardiovascular syphilis found among 9,200 syphilitic patients discovered through a serological survey of 331,939 industrial workers of São Paulo. The cardiovascular localization was found most frequently among patients between 36 and 55 years of age (132 patients, or 67.3%). Among the 196 patients, 0.7% had an uncomplicated aortitis and 1.4% a complicated aortitis. Uncomplicated aortitis was more frequent than aortic insufficiency and aortic aneurysm among patients in the age group 36 to 55 years (38.5%, 23.3%, and 20.0% respectively). The frequency of uncomplicated aortitis diminished with the age while that of aortic insufficiency and aortic aneurysm increased among patients 56 or over (10.7%, 27.2%, and 33.3% respectively).

Cardiovascular syphilis was more frequent among men than among women (2.5:1), and uncomplicated aortitis and aortic aneurysm were more frequent among women (40.9% and 18.1% respectively) than among men (32.1% and 11.4%). Aortic insufficiency was more frequent among men than among women (56.8% and 40.9%). No significant difference was found in uncomplicated aortitis in white and colored patients (32.8% and 34.0%). The frequency of cardiovascular syphilis in younger age groups was higher in colored than in white patients. Most patients had their cardiovascular syphilis diagnosed from 11 to 30 years after the initial lesion. Uncomplicated aortitis was found with highest frequency in the second decade of the infection, while the highest frequency of aortic insufficiency and aortic aneurysm was found in the third decade. Of the 196 patients with cardiovascular syphilis, 23% also had involvement of the central nervous system. Of these patients 24% showed symptoms interfering with their professional activity.

ITALY

Liver Regeneration After Hepatectomy.—A. Dagradi and co-workers *(Chirurgia e patologia sperimentale,* vol. 6, 1958) used rats in a study of hepatic regenerative phenomena because these animals survive the removal of 67% of the liver. Hepatic regeneration in rats takes place for one week after subtotal resection. A premitotic period of regeneration lasts 24 hours; a mitotic period lasts till the end of the third day; and a postmitotic period lasts until the end of the quantitative recovery of the liver. The postmitotic period may be further subdivided into a slow revival during the second week of the regenerative process which is related to the recovery of the body-weight of the animal, which *falls in the first week because of undernutrition*

The items in these letters are contributed by regular correspondents in the various foreign countries.

caused by the operation and not by a specific regenerative stimulus. The fundamental process of liver regeneration lies in nucleic acid synthesis and cellular division. Its cause may be a decrease of the substance produced by the hepatic cells which normally inhibits proliferation.

Heparin Hypersensitivity.—P. Ottaviani and co-workers *(Progresso medico*, Sept. 15, 1958), having studied the heparin hypersensitivity syndrome, pointed out that it is characterized by localized allergic manifestations, pulmonary edema, and cardiovascular failure which may result in shock. Using various heparin preparations in guinea pigs the authors found that the antigenic property of heparin is due to the drug itself and cannot be referred to other substances contained in various heparin preparations. In patients in whom heparin therapy is necessary, the treatment can be started again after specific desensitization.

Renal Function After Nephrectomy.—P. Zucchelli and co-workers *(Riforma medica*, vol. 43, Oct. 25, 1958) studied renal function after the removal of one kidney in 19 patients. Glomerular filtration exceeded 100 cc. per minute only in patients who had been operated on at least six months earlier. The compensatory adaption of the flow of plasma paralleled the return of glomerular filtration.

NORWAY

Treatment by Manipulation.—A series of discussions reported in *Nordisk medicin* for Sept. 25 showed how much is being done by orthopedists and other physicians to rescue manipulative treatment from the various healing cults, to study its basic principles, and to exploit what is best in it under scientific safeguards. The discussions were prompted by a study by Dr. E. H. Schiötz that ran serially in *Tidsskrift for den norske lægeforenning*. In January, 1957, the national health insurance authorities decided to defray some of the charges of the practitioners of manipulative treatment. They must, however, have been duly recognized as such by a board of examiners, and the physician recommending manipulative treatment to the patient must be a specialist in orthopedics, neurology, or rheumatology. To be recognized as such, the manipulative practitioner must have had at least three years' training in this field, and he must have satisfied a board of examiners on which the medical profession was substantially represented.

Stature of Norwegians.—Professor A. Sundal (*Nasjonalforeningen mot tuberkulosen for folkehelsen*, vol. 48, 1958) presented figures showing that improvement of environment has not only reduced infant mortality but has also added to individual weight and stature. In 1900 there were 81 deaths during the first year of life per 1,000 live births, whereas the corresponding figure for 1954 was 21.4. In 1956 17,000 children between the ages of 0 and 15 in Bergen were compared with 25,000 children in Oslo who were the same age in 1931. In the matter of height and weight the 10-year-old boys and girls in Bergen were equal to the 11½-year-old boys and girls of Oslo. This upward shift of stature was also demonstrable in military draftees, for between 1910 and 1949 the mean height of recruits increased from 171 to 175.6 cm. (5 ft. 7 in. to 5 ft. 9 in.). Much of the credit for this change belongs to the child welfare stations in operation during the last 40 years.

Trichinosis.—Dr. T. Flatmark (*Tidsskrift for den norske lægeforening*, Sept. 1, 1958) stated that the German invasion of Norway in 1940 led to outbreaks of trichinosis in this country and to sanitary measures which are still in force. In the autumn of 1940, 668 German soldiers and 10 Norwegian civilians fell ill, but there was only one death (a German) and 67% of all the cases were moderately severe or mild. Strict preventive measures are now enforced. In 1943 serologic tests for trichinosis in 15 German soldiers who had eaten a polar bear proved positive, giving support to the opinion that 60% of such bears were thus infected. While trichinosis in man has become rare in Norway, the demonstration of this disease in swine is impressive, with as many as 66 such cases in one county between 1940 and 1954. The total for the country as a whole was 332 cases in swine publicly or privately slaughtered in the same period. Flatmark suggested that trichinosis in Norwegians may be less rare than is suspected, since it is likely to run a mild course and thus escape detection.

Norwegian Medical Society.—Just 125 years ago an epidemic of cholera stirred 16 men, including 2 apothecaries, to meet it by banding themselves together into a body designed to combat it. The membership of this medical society was not numerically impressive, but when it celebrated its 50th birthday it could boast a membership of 192. Now it has soared to about 500. At first the modest ambition of this body was to act as a discussion club and to air the opinions of its members on current medical problems, and its earlier records reveal a certain, and doubtless inevitable, ambiguity of outlook and paucity of scientific data. At present the Norwegian Medical Society has become the forum before which scientific data are carefully scrutinized. In the presence of King Olav, the chairman of the Society, Professor H. A. Salvesen, outlined the achievements made by medical science in the past 25 years. In no other 25-year period in the history of man has such progress been made as in the last quarter of a century.

Interval Operation for Cholecystitis.—Hertzberg and Nilssen (*Journal of the Oslo City Hospitals*, vol. 8, September, 1958) discussed the comparative merits of immediate operation for acute cholecystitis and conservative treatment followed by operation later. Their material consisted of 406 unselected patients treated in the 11-year period 1945-1955 at Ullevaal hospital with a mortality of 7.4% (30 deaths). There were no deaths among the 77 patients under the age of 50. The most frequent but least serious complication was pancreatitis, observed in 131 patients; rupture of the gallbladder with peritonitis occurred in 20; and stones of the common bile duct with persistent cholangitis and jaundice in 23. Interval cholecystectomy was performed on 123 patients with an average age of 55 with no deaths. There were 169 patients with an average age of 57 who refused the recommended operation. Questionnaires subsequently addressed to them yielded data about 106 of them. Among them were 2 who had died of their disease, 9 who had been operated on elsewhere, 58 who still had symptoms, and 37 who had become symptom-free. It was concluded that immediate operation might be preferable after the ages of 60 or 70. A disadvantage of interval operation was that many patients who were advised to have it did not do so. Penicillin alone or with streptomycin and broad-spectrum antibiotics seemed to be about equally effective in reducing mortality. Vital indications may warrant immediate operation in the acute stage of the disease.

SWEDEN

Histamine Determination.—Dunér and Pernow (*Scandinavian Journal of Clinical and Laboratory Investigation*, vol. 10, 1958) reported a modified technique for determination of histamine in the blood, based on their earlier method for extracting histamine from the urine. The content of histamine in serum ranged from 0.6 to 2.8 mcg. per 100 ml. of blood (mean 1.29). The corresponding values for blood cells were 1.0 to 4.6 (mean 2.66). The specificity of the method was studied by passing mixtures of histamine and other smooth-muscle-stimulating agents such as acetylcholine, 5-hydroxytryptamine (5 HT), substance P, and potassium through the Amberlite IRC-50 column. At the subsequent biological assay of the eluates, 5 HT and potassium were found in the same fractions as the histamine. Because of this finding the earlier method for extraction and determination of histamine was modified by a treatment of the eluates with alcohol acetone in order to precipitate the salts, and by addition of dihydroergotamine to the bath-fluid in order to make the intestine insensitive to 5 HT. Administration of antihistaminic promethazine renders the biological assay of histamine impossible because of excretion of promethazine in the urine, but the promethazine can be eliminated by extraction with ether. The excretion of histamine in the urine was found not to be influenced by oral administration of promethazine.

Enzyme Patterns in Serum and Tissue Extracts.—The proportions of serum glutamic-oxalacetic transaminase (SGO-T), serum glutamic-pyruvic transaminase (SGP-T), and serum lactic dehydrogenase (SLD) in patients with acute myocardial infarction were found by S. Linde (*Scandinavian Journal of Clinical and Laboratory Investigation*, vol. 10, 1958) to be about the same as those of these enzymes in muscle extracts. Linde reported on the maximal increase in the serum enzyme activities in 32 patients with myocardial infarction and compared it with the enzyme activities in striated muscles from 10 healthy human beings and noted that the proportions corresponded fairly well. The relative proportions between the serum enzyme activities in 22 patients with epidemic hepatitis did not correspond to the enzyme activities in hepatic tissues from 10 healthy human beings, where the SCP-T activity is much less than the SGO-T activity. In eight rabbits in which hepatic damage was produced with carbon tetrachloride and in human beings with hepatic injury due to acute alcoholic intoxication the proportions between the different serum enzymes were about the same as in hepatic tissue.

The Blood-Brain Phenomenon.—Ricardo Edström in *Acta psychiatrica et neurologica scandinavica* (vol. 33, 1958) stated that since there seems to be a virtual lack of extravascular, extracellular space within the brain, it had been suggested that the well-known restriction to transport from the blood may not need the assumption of a specific blood-brain barrier. The restriction may merely be a combined effect of the obstacles offered by a normal capillary wall and the closely adjacent cell membranes. The transfer thus takes place from the blood directed into the intracellular space and not to an extracellular, extravascular space, as is the case in other organs.

Pneumoencephalographic Studies in Epileptics.—The occurrence of pneumoencephalographic signs of atrophy was investigated by B. Falk and coworkers (*Acta psychiatrica et neurologica scandinavica*, vol. 33, 1958) in two groups of ambulant epileptics. The disease had been of long duration in most patients, and the frequency of fits had been moderate to low. In 20 patients with central epilepsy 5 showed slightly widened lateral ventricles. No definite dilatation of sulci was found. In 25 patients with temporal lobe epilepsy 4 showed a slight dilatation of the lateral ventricles, and the gyri in various parts of the cortex were more or less dilated in 11. The temporal horns showed a slight dilatation in 4. The frequency of grand mal seizures did not in the cases reported seem to have any relation to the occurrence of atrophy as evidenced by pneumoencephalography.

Asymptomatic Myocarditis.—In order to determine the possible presence of asymptomatic myocarditis after Asian influenza, Levander and Rigner (*Militär Hälsovård*, vol. 2, 1958) examined 85 conscripts who were apparently in excellent health by electrocardiography in the recumbent and the erect position two to six weeks after the onset of Asian influenza; 75 who had not been ill were used as controls. Three of the patients showed changes in the S-T segment and T-waves strongly suggesting myocarditis or perimyocarditis while the controls did not show these changes. No other subjective or objective cardiac symptoms were observed in these three patients. Radiography of the heart did not reveal any abnormality and physical working capacity was normal. In one patient the electrocardiographic changes disappeared within two weeks. A relationship between myocarditis and influenza in this patient was suggested. In the other two patients the electrocardiographic changes persisted but showed a tendency to regress during an observation period of 11 weeks, their relation to the preexisting influenza being therefore doubtful.

A relatively high frequency coronary sinus rhythm was observed in one of the patients, and in the control group one of the men showed a low frequency ventricular pacemaker of the passive type. The ECGs taken in the erect position revealed pathological changes which were more marked than those shown in the ECGs taken in the recumbent position. ECGs taken in the erect position were recommended as a valuable and simple supplementary method of examination. These findings support the view expressed by earlier workers that asymptomatic myocarditis is not uncommon and should be kept in mind.

Acute Intermittent Porphyria.—Nettelbladt and Nisell (*Opuscula Medica*, vol. 3, 1958) reported a series of 24 patients with porphyrinuria, 13 of whom had acute intermittent porphyria. All of them suffered from abdominal pain and in all but one dark urine was passed. Most of the attacks were benign with spontaneous recovery, but in two the course was protracted. Precipitating factors in some of the attacks were ingestion of barbiturate, infection, and pregnancy. In the same issue Gösta von Reis reported that among these 13 patients 7 had psychic changes, 4 showing hysterical symptoms and 2 oligophrenia. Neurological symptoms were found in seven patients, four showing signs of peripheral neuron lesions and two severe motor disturbances including tetraplegia and diaphragmatic paralysis. Landry's ascending paralysis was not observed, but three patients had epileptic seizures.

Chemotherapy in Cancer.—S. Kallner (*Opuscula Medica*, vol. 3, 1958) stated that conventional methods of treating cancer show a low cure rate, but busulfan has given good results in patients with granulocytic leukemia. The results of treatment of cancer with ethyleneimine quinone have varied markedly, but in some patients the primary tumors and metastases decreased or disappeared. Striking effects were particularly noted in some patients with pulmonary carcinoma.

Staphylococcic Infections in a Hospital.—An epidemic of staphylococcic infection occurring on the neurosurgical ward of Södersjukhuset Hospital in Stockholm was described by Ragnar Frykholm (*Opuscula Medica*, vol. 3, 1958). Of five who had had brain surgery, only one survived. A separation into clean and infected wards was recommended. Patients treated with antibiotics were regarded as potential carriers of infection. Prophylactic antibiotic therapy was no longer used. In a general surgical ward Forsgren and Varenius (same issue) found that about 50% of the ward personnel were nose and throat carriers of Staphylococcus pyogenes var. aureus. Of these carriers 31% had staphylococci with antibiograms and phage patterns that were identical with those of six patients who developed staphylococcic infections in the hospital. In the floor dust and room air around the patients identical staphylococci were found. A reduction in the use of antibiotic therapy and general hygienic measures formerly routine was adopted and two months later no new infection had occurred among the patients and the original pathogenic phage types could no longer be found among the personnel or on the premises.

Treatment of Tuberculosis.—Dahlström and Uggla (*Opuscula Medica*, vol. 3, 1958) stated that the negative attitude towards the use of ACTH and cortisone in tuberculosis was based on results of animal experiments. The authors made a controlled investigation on 15 patients who were treated with cortisone and specific chemotherapeutic agents. They obtained good results and they emphasized that an absolute prerequisite for using cortisone in the treatment of tuberculosis was simultaneous and efficient chemotherapy.

Staphylococcic Septicemia.—Georg Matell (*Opuscula Medica*, vol. 3, 1958) successfully treated two patients who had staphylococcic septicemia with liberal use of antibiotics, causing metastatic pneumonia. He believed the development of resistant strains of staphylococci had changed the clinical findings in severe staphylococcic infections, and these had supplanted pneumococcic infections as the terminal illness in elderly patients. Staphylococcic septicemia in its classical form has become rare.

The prognosis of the classical form was probably much better than was generally believed. The two patients reported, a 30-year-old woman and a 46-year-old man, both with severe sepsis after incision of carbuncles and with pulmonary involvement, were cured, one with terramycin and oxytetracycline and the other with oxytetracycline and erythromycin in combination with oleandomycin tetracycline.

UNITED KINGDOM

Salicylates and Gastrointestinal Hemorrhage.—In a series of 103 patients with hematemesis and/or melena, 55 had taken salicylates within the preceding 72 hours, compared with only 17 of 103 patients complaining of dyspepsia but not of gastrointestinal bleeding, according to Alvarez and Summerskill (*Lancet* 2:920, 1958). There was an even more striking difference between the two groups as regards the taking of salicylates in the 24 hours preceding hemorrhage or the onset of dyspeptic symptoms: 49 of those with bleeding, and only 7 of those complaining of dyspepsia. Occult blood loss in the stools occurred during periods of taking salicylates in about 50% of patients with peptic ulcer or x-ray negative dyspepsia and in a comparable percentage of controls. Both soluble and insoluble aspirin caused occult bleeding, but nonsalicylate analgesics (e. g., phenacetin) did not influence the occult blood content of the feces.

A Hazard of Needling.—Gibson and Norris (*Lancet* 2:983, 1958) reported that when a hollow needle is thrust through the skin, it cores out a fragment of tissue in 69% of cases. The size of the needle has little to do with it, except that the core of skin is roughly proportional to the size of the needle's lumen. It is agreed, however, that if skin preparation is thorough, there is no reason to condemn the routine use of open-ended injection needles.

Prostatic Cancer.—The cytological examination of smears can be a valuable aid in the diagnosis of carcinoma of the prostate, according to Joseph Bamforth (*Ann. Roy. Coll. Surgeons England* 23: 248, 1958). Of 513 specimens he received for examination from different sources, 177 proved to be inadequate as they did not contain sufficient prostatic epithelial cells for critical examination. Of the remaining 336 examined by cytology, 176 were reported as negative and 160 as positive or "suspicious." Of the latter 70 were confirmed by histological examination or by the development of metastases detected radiologically, and 90 were classified as undetermined. Most of these were regarded on clinical grounds as being definite cases of carcinoma. In some there were high values for serum acid phosphatase. Some might be cases of latent carcinoma.

Artificial Insemination.—The Eugenics Society has set up an A. I. D. council to consider the present status and genetic, medical, legal, and social potentialities of artificial insemination by a donor. What the council has in mind is the maintenance of a permanent committee which will at all times have a record of available data on such cases in this country, with all medical and scientific information relevant thereto. The following opinion has been expressed by the solicitor of the Medical Protection Society: "Although artificial insemination must by its very nature provide a source of legal complications affecting questions of legitimacy, inheritance, nullity, and divorce, it should not involve a doctor in any difficulty so long as he acts with care and discretion. The practitioner asked to carry out artificial insemination will be faced with no legal problem if the donor is to be the husband (A. I. H.). If the donor is to be someone other than the husband (A. I. D.), the position should be fully explained to the husband and the wife, and a request and consent in writing signed by both should be obtained."

Hospital Costs.—A new method of accounting was used in about 200 of the hospitals in the National Health Service (Hospital Costing Returns for Year Ended 31st March, Her Majesty's Stationery Office, 1958). Under the new system the costs are analyzed by departments, such as wards, works and maintenance, medical services, laundry, and administration. Hospital outpatient expenditure is now listed separately, whereas formerly it was estimated on the assumption that five outpatient attendances represented one inpatient day. The new estimates show that the average cost of an outpatient attendance in England and Wales is $2.40. In provincial teaching hospitals it is nearly $2.60, and in the London teaching hospitals it is $3.03. The average cost of a new outpatient in the three types of hospitals is $7.40, $7.50, and $12.60 respectively. The higher cost in London teaching hospitals is not because more elaborate diagnostic techniques are used, or that salaries are higher, but because the outpatient attendances are lower. Of the London teaching hospitals, St. George's Hospital has the highest inpatient cost, $109.50 per week, compared with $80.20 for the average London hospital, and $94 for the London teaching hospital.

Institute of Orthopedics.—A new research block for the Institute of Orthopedics was opened at Stanmore, where the rural branch of the National Orthopedic Hospital is situated. The opening ceremony was performed by Sir Henry Dale, of the Wellcome Trust, which contributed $120,000 toward the building. The institute was established in 1946 in the Royal National Orthopedic Hospital in London, where it occupied one of the floors. A metabolic unit was added in 1951, and a department of biochemistry in 1952. Laboratories for pathology and clinical research and an orthopedic museum were subsequently incorporated. The opening of the new block at Stanmore completed the institute's building program. The department of biochemistry is headed by Dr. P. Walker, who is examining enzymes associated with the breakdown of hyaluronic acid and chondroitin sulfate. Dr. C. Lack, who directs the division of clinical pathology and bacteriology, is studying plasminogen, the preparation and properties of staphylokinase, serologic tests for staphylococcic infection, and the mechanism whereby cartilage is destroyed in suppurative arthritis. Dr. Angus McPherson is studying viscerosomatic spinal reflexes; Dr. Hubert Sissons is studying bone disorders and muscle atrophy; and Dr. John Scales is examining the fate of metallic implants in the body, the design of prostheses, and the applications of plastics in orthopedics.

Control of Pain.—Although phenol achieved notoriety in a recent court case as a cause of damage to the spinal cord, Brown claims that if it is dissolved in anhydrous glycerol, or in the contrast agent iophendylate, and injected intraspinally, it relieves intractable pain due to spinal cord irritation without causing any apparent harm (*Lancet* 2:975, 1958). He injected intraspinally 2 ml. of a 5% solution of phenol in one of the solvents at the level of the roots carrying pain from a malignant lesion. By accurate positioning of the patient the hyperbaric phenol solution was concentrated at the chosen level and kept there for about 30 minutes. In the lumbar and sacral regions injection and positioning were relatively easy, but in the midthoracic and cervical regions fluoroscopy was required. Treatments were given every two days. Pain was relieved within 20 minutes by this procedure. Sensation of touch, pinprick, vibration, proprioception, temperature, and tendon and muscle pain were unimpaired. Immediately after the injection a sensation of coldness was followed by analgesia and weakness of the affected limb, which lasted for about 20 minutes, then motor power and sensation gradually recovered over the next 24 hours. Superficial and deep reflexes vanished and did not return. While resting muscle tone was permanently greatly reduced, voluntary motor power was unaffected.

Fifty-five patients with severe intractable pain were treated by this method. Of 38 with pain due to cancer, 30 were relieved, but in only 5 of 17 patients with pain of nonmalignant origin was analgesia obtained. Although no local reaction to the injected phenol was seen at the autopsy of some of the cancer patients, four had a well-marked arachnoiditis when the spinal cord was exposed two to four weeks after treatment. So far, however, no patient has shown any clinical evidence of adhesive or obliterative arachnoiditis. The site of the action of the phenol appeared to be the posterior-root ganglion or the region of the proximal neuroganglionic junction. The patients have been under observation for periods up to 21 months. A much longer follow-up period is required to exclude the possibility of serious delayed neurological complications, which may take months, or even years, to develop, and once established cannot be reversed. For this reason Brown suggested that for the time being intraspinally administered phenol should be used mainly for treating the pain of malignant disease.

Mass Radiography.—The Corporation of Glasgow published the results of its mass radiography campaign, during which 714,915 people or 76% of the town's population were x-rayed. In five weeks 2,755 cases of active pulmonary tuberculosis or 3.8 per 1,000 in those examined were detected. A further 5,379 cases of tuberculosis of doubtful activity were brought to light. The detection rate was greater in men than in women (4.8 to 2.8 per 1,000), due to the high incidence of the disease in older men. In the last 20 years tuberculosis has been diagnosed mainly in the young adult and has largely escaped detection in middle-aged and elderly persons. It is remarkable that such a large number of people were x-rayed. The success was attributed to good publicity and a short but intensive campaign, which was directed by a special committee, including newspaper and cinema men and representatives of the BBC. A million pieces of publicity material, including 100,000 posters, were issued. Every bus and streetcar and nearly every shop carried a poster. Competitions were organized and prizes offered, although the serious side, with a full explanation of the campaign, was not neglected. Press, radio, and cinema were used to impress on the people of Glasgow the importance of the project. It was thought that if more units had been available over 80% of the population would have been x-rayed. Among the 6,576 contracts x-rayed after the campaign only 17 new cases of tuberculosis were found. The total cost of the scheme was $320,000 or 44 cents per person examined. The cost of detecting a new and active case of tuberculosis was about $125. Publicity cost $47,600 or 6.7 cents per film. The organizers believed that the cost of the campaign was well justified.

CORRESPONDENCE

POSTMORTEM DIAGNOSIS OF INSULIN SHOCK

To the Editor:—In the article by Birkinshaw and co-workers (Investigations in a Case of Murder by Insulin Poisoning, *Brit. M. J.* 2:463-468 [Aug. 23] 1958) discussed in the Foreign Letters section of The Journal (168:811 [Oct. 11] 1958) detection, identification, and quantitation of insulin were ingeniously achieved in tissue extracts from sites of needle marks in the victim's buttocks. However, in spite of large amounts of insulin in the body of the victim, paradoxically, not hypoglycemia but a hyperglycemia of 210 mg. per 100 ml. was demonstrated about six hours after death. Postmortem chemistry, so far, has been applied mainly as aid in *autopsy diagnosis of diabetes mellitus (Hamilton-*Patterson and Johnson, *J. Path. & Bact.* 50:473-482 [May] 1940; Tonge and Wannan, *M. J. Australia* 1:439-447 [April 2] 1949; and Naumann, *Am. J. Clin. Path.* 20:314-324 [April] 1950) but *rarely of insulin* shock. Proof of antemortem insulin effect by postmortem glucose values is difficult, since glycolysis soon after death lowers glucose concentrations *except in the inferior vena cava and right heart* blood, where it may greatly increase by diffusion of glucose liberated through glycogenolysis in the liver. Postmortem glycolysis, but less marked and erratic, is present also in the cerebrospinal fluid, which is subject neither to interference by clotting nor to that by non-sugar-reducing substances. The decrease of cerebrospinal fluid glucose (see table) shows the main drop in concentration after the first hour post mortem and irregular rise between the 3rd and 10th hour.

Postmortem Cerebrospinal Fluid Glucose Level, Determined by the Folin-Wu Method, One to Ten Hours After Death

Hours Post Mortem	Cases, No.	Levels, Mg./100 Ml. Average	Range
1	11	90	63-134
2	9	55	30-80
3	15	49	23-84
6	5	58	42-76
10	6	29	14-35

Based on several articles (Naumann, *Arch. Path.* 47:70-77 [Jan.] 1949; *Am. J. Clin. Path.* 26:495-505 [May] 1956; Queries and Minor Notes, *J. A. M. A.* 157:780 [Feb. 26] 1955; *Proc. Soc. Exper. Biol. & Med.* 98:16-18, 1958), a presentation of conditions and criteria for the postmortem diagnosis of insulin shock may be made as follows: 1. Only cerebrospinal fluid, except in patients with meningitis, and not blood should be used for postmortem glucose level determinations, especially when an insulin reaction is suspected for reasons given above. 2. Glucose values found must be low enough—50% or less of lower ranges observed after death (see *table)—and analytical errors small enough by duplicate* determinations of concentrated solutions to prevent misinterpretation due to chance variation. 3. Cerebrospinal fluid glucose levels of 30 ± 0.5 mg. per 100 ml. or less in the third hour may be considered presumptive evidence of insulin shock, provided specimens are analyzed promptly. 4. Values of specimens taken later than three hours after death are difficult to interpret but if low enough may be considered confirmatory evidence of insulin shock.

In the case of Birkinshaw and co-workers the specimen of "mixed heart blood" presumably contained right heart blood with high glucose level due to diffusion of glucose derived from liver glycogen. Although conclusive evidence of insulin effect could not have been secured six hours after death, a low cerebrospinal fluid glucose value, nevertheless, may have served as corroborative evidence. In one of my own cases of death due to accidental overdose of insulin, the cerebrospinal fluid glucose level was found to be 19 mg. per 100 ml. three hours after death, a result consistent with a postmortem diagnosis of insulin shock.

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ASSOCIATION OF CHOLELITHIASIS, HIATUS HERNIA, AND DIVERTICULOSIS COLI

To the Editor:—In The Journal (168:257-261 [Sept. 20] 1958) Foster and Knutson gave some interesting data regarding the frequency of occurrence of the association of cholelithiasis, hiatus hernia, and diverticulosis coli in a hospital population. This frequency was found to be far greater than that calculated as due to random coincidence. In this calculation, however, there seem to be some possible errors which could partly or wholly account for the results of the study.

First, there is a possibility of error due to differences in probability of admission to hospital for patients with the triad and patients with the single conditions. We believe it to be generally agreed that the three single conditions under study may occur without giving rise to symptoms. This implies that some patients with one or more components of the triad are not referred to hospital. Even when ideal conditions exist and all patients with symptoms of at least one of the components seek medical advice and are referred to hospital, those without symptoms will stay behind. This also implies that occurrence of two or three components of the triad in the same patient could give this patient an increased probability of admission to hospital, simply because of the increased probability of symptoms. It also seems to be generally agreed that the three components can give rise to similar symptoms. Therefore hospital admission of patients with symptomless components in association with one or two other components with symptoms will imply a high probability that also the symptomless component is detected. This will certainly be the case when doctors start assuming an etiological association between the components of the triad and when finding one of the components make the necessary radiologic examinations to detect the other components. Therefore, even if no association exists between the components of the triad, the frequency of occurrence of the triad in a hospital population is likely to be greater than random coincidence as calculated by multiplication of the frequencies of the single diseases in the hospital population. This will be the case even under the ideal conditions mentioned before (Berkson, *J. Biometrics Bull.* 2:47, 1946).

Second, there is a possibility of error due to selection of the patients subjected to the different radiologic examinations. When only the hospital population under investigation (the 2,020 patients studied) is considered, the calculation of the P values of the different diseases is hard to understand. The method of estimating the P values, applied by Foster and Knutson, is valid only under the assumption that the choice between the three radiologic examinations has been made strictly at random. The article does not give the impression that this has been the case. The question arises as to why 713 patients were subjected to all three radiologic examinations. Possibly the answer to this question is that various symptoms motivated more extensive radiologic examination. If that is so, it may be less surprising to find a high incidence of double and triple associations among patients so selected.

Third, there is a possibility of error due to age differences in the incidence of the three diseases. As the incidence of the three components is known to rise with increasing age, the high incidence of the triad might be partly due to this. The fact that the mean age of the patients with the triad was found to be higher than the mean ages of the patients with one of the components is in accordance with this assumption. Such association, however, lacks biological significance.

The study of Foster and Knutson has the merit that it draws attention to the difficulties facing the surgeon when trying to evaluate the proper therapy in each single case of a double or triple association. It is a pity, however, that the authors have not investigated their material from the selection point of view. Their view on possible etiological factors in the association of the three diseases is very valuable. It seems, however, that the association of the three components of the triad cannot be proved on the basis of the statistical data presented.

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To the Editor:—I am pleased that doctors van der Linden and Taube have critically analyzed our figures and believe that their statements are well worth publishing. Our study was not primarily oriented to statistics but designed rather to alert clinicians as to the frequency of the triple association. To further amplify our viewpoint, I shall comment on the salient points raised in the critique.

A series of cases studied by x-ray could not readily be obtained outside a clinic or hospital population. The approximate 15% asymptomatic patients with the triad would not heavily weight a nonhospital population in favor of chance. The incidence of the respective single conditions in our series is not significantly greater than those of any other report. Hence, the probability value obtained by multiplication of the percentages should be acceptable. The 713 patients having all three roentgenographic studies happened to fall in this category on the basis of the usual indications as determined by several examiners. This was not a study to find the triad cases but largely a retrospective calculation.

We would be happy if others would attempt to test our conclusions. It would be interesting to see the results of an ideal statistical study.

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FREEDOM FOR THE PROFESSIONS

To the Editor:—On June 14, 1958, Rear Adm. H. G. Rickover gave an address to the graduating class of the Stevens Institute of Technology in which he paid some very handsome compliments to the professional principles under which the American Medical Association operates. In particular, he noted the advantages of a fee for service, in preference to salary, in compensation of professional personnel. He pointed out that this is one of the strong methods of resisting the lay control of professional acts by administrators. In general, he is advising those who would make a full-fledged profession of engineering to follow the medical example.

Some weeks ago the *Manchester Guardian* called attention to the fact that physicians were leaving East Germany in large numbers, because the East German government had denied their children the right to be admitted to the universities, since they were not members of the working classes. In the issue of Sept. 25, 1958, it appears that the East German government has backed down in the face of a great shortage of physicians. They now offer to give the children of physicians rights equal to those of workers and farmers in obtaining entrance to the universities and technical colleges.

It was also noted that physicians will be allowed to carry on their independent practices, and there will be no compulsion to work on state panels. Physicians will now be allowed to travel freely in West Germany to attend congresses and meetings. They will be allowed to practice their profession, irrespective of whether they bind themselves to follow the precepts of dialectical materialism. This is an example of the strength of a strong professional organization.

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TORT LIABILITY OF CHARITABLE HOSPITALS TO PATIENTS

To the Editor:—Although the review on "Tort Liability of Charitable Hospitals to Patients" in The Journal (168:788-789 [Oct. 11] 1958) provides a valuable survey of the law in the several states, it may be prudent to bring attention to an inaccuracy which appears in the state-by-state schedule appended to the digest. New Jersey is there represented as a jurisdiction which supports "full liability." For authority, the collator cites *Collopy v. Neward Eye & Ear Infirmary,* 141 A. (2d.) 276 (1958).

The Collopy case was decided April 28, 1958, and it is true that the Supreme Court of New Jersey there rejected the former New Jersey rule, which for 33 years had denied recovery to patients damaged through the negligence of the agents of a charitable hospital. Three months later, however, July 22, 1958, the governor of New Jersey signed into law an act of the legislature which restored, in part, the earlier New Jersey judicial rule of charitable immunity, providing as follows:

> 1. No nonprofit corporation, society or association organized exclusively for religious, charitable, educational or hospital purposes shall, except as is hereinafter set forth, be liable to respond in damages to any person who shall suffer damage from the negligence of any agent or servant of such corporation, society or association, where such person is a beneficiary . . . of such nonprofit corporation, society, or corporation; . . . *Chapter 131, P.L. 1958.*

The mentioned exception permits recovery against "any nonprofit corporation, society or association organized exclusively for hospital purposes . . . to an amount not exceeding $10,000.00 . . ." By express language, the statute expires June 30, 1959. "Full liability" of charitable hospitals in New Jersey for the negligence of agents is not, then, the current law. Although liability does clearly exist, no recovery can exceed $10,000.

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THE FAMILY DOCTOR

To the Editor:—In the correspondence section of The Journal, Dec. 6, 1958, page 1929, an interesting letter by Dr. Leo J. DeBacker appears in reference to an article by Dr. Wheatley. Both doctors suggested remedies for the deplorable situation of boredom in which some pediatricians seem to find themselves. It is remarkable to me that an obvious solution has not occurred to either author. It seems self-evident that our medical school faculties should orient themselves more strongly to inducing young men to go into the field of general practice rather than glamorizing the specialties. Rather than the pediatrician being the family doctor of the future, I believe that the family doctor is the qualified man in the present and the future. If any young medical student will switch his interest from pediatrics to general practice, I can guarantee he may get tired, but never bored.

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MEDICAL LITERATURE ABSTRACTS

INTERNAL MEDICINE

Acute Myocardial Ischaemia: Significance of Plasma-Transaminase Activity. A. J. Goble and E. N. O'Brien. Lancet 2:873-877 (Oct. 25) 1958 [London].

The authors performed serial estimations of glutamic oxalacetic transaminase activity of plasma (P. G. O. T.) with the aid of a modification of Karmen's spectrophotometric method in 25 normal persons and in 20 patients with a history of angina pectoris or previous myocardial infarction who were at rest and free from pain in the cardiac department of the Royal Melbourne Hospital in Melbourne, Australia. Serial estimations of P. G. O. T. activity also were carried out in the same hospital in 18 patients with severe attacks of cardiac pain unassociated with clinical and electrocardiographic evidence of recent myocardial infarction. In the 25 normal persons and in the 20 patients with known ischemic heart disease who were resting and free from pain, the individual maximum range of serial P. G. O. T. levels was 10 units or less with one exception. Rises of P. G. O. T. levels beyond an individual highest-to-lowest range limit of 15 units were therefore regarded as abnormal, and between 10 and 15 units as probably abnormal. Of the 18 patients with severe attacks of typical cardiac pain, 10 had isolated attacks of pain and 8 had repeated attacks of pain extending over more than 2 weeks; 4 of the 10 patients and all the 8 patients had increased P. G. O. T. levels. A single rise in P. G. O. T. activity occurred in the 4 patients, and irregular or repeated rises in P. G. O. T. levels were observed in the 8 patients. The patterns of P. G. O. T. activity thus indicated single episodes of necrosis in some patients with isolated attacks of pain and similar but repeated episodes in those with attacks of pain recurring for weeks. There was a subsequent rise in the erythrocyte sedimentation rate in 11 of these 12 patients. In none of the 18 patients did the temperature rise, or leukocytosis, persistent fall in blood pressure, or cardiac failure occur. The electrocardiograms obtained from these patients revealed depression of the S-T segments or inversion of T waves, whether necrosis was demonstrable or not. The severity and duration of pain, associated dyspnea, sweating, and temporary fall in blood pressure, and electrocardiography proved to be unreliable guides to necrosis associated with severe myocardial ischemia.

Plasma-glutamic-oxalacetic-transaminase activity is a sensitive index of myocardial necrosis. A new descriptive terminology is both possible and necessary, recognizing that cardiac pain, irrespective of its duration or severity, indicates myocardial ischemia, that rises of erythrocyte sedimentation rate and P. G. O. T. levels indicate myocardial necrosis, and that electrocardiographic changes indicate the localization of the myocardial ischemia or necrosis. It should also be recognized that repeated small attacks of myocardial necrosis may summate to produce the electrocardiographic pattern of transmural myocardial infarction.

Successful Treatment of Quinidine and Procaine Amide Intoxication: Report of Three Cases. F. Wasserman, L. Brodsky, M. M. Dick and others. New England J. Med. 259:797-802 (Oct. 23) 1958 [Boston].

Studies made by the authors in laboratory animals had demonstrated the efficacy of molar sodium lactate in reversing toxic electrocardiographic and blood pressure changes resulting from quinidine and procainamide. They report on 3 patients whose histories illustrate the successful clinical application of their observations on animals. Toxic effects from quinidine and procainamide are relatively uncommon, but they may result from increased sensitivity to the drugs or from overdosage. The electrocardiographic changes of quinidine and procainamide intoxication consist of sinoatrial slowing, followed by sinus pauses, sinus arrhythmias, progressive QRS widening, prolongation of the P-R and Q-T intervals, RS-T-segment depression and T-wave changes; in addition defects of interatrial conduction, leading to partial or complete interatrial block, have been observed. A late manifestation consists of an atrioventricular nodal rhythm that terminates in either ventricular fibrillation or ventricular standstill. More commonly recognized clinical signs and symptoms of intoxication with quinidine or procainamide are nausea, vomiting, diarrhea, vertigo, tinnitus, and hypotension. Attempts have been made to correlate plasma quini-

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The place of publication of the periodicals appears in brackets preceding each abstract.

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dine levels with therapeutic effects and toxic manifestations. The presence of congestive heart failure and renal impairment appears to increase the likelihood of cardiotoxicity from quinidine at lower plasma concentrations.

The first of the 3 patients, who had a plasma quinidine level of 5.1 mg. per liter, became hypotensive, and sinus bradycardia developed. The second patient with congestive heart failure, acidosis, and azotemia secondary to renal insufficiency showed severe electrocardiographic and clinical signs of quinidine intoxication with a plasma quinidine level of 6.3 mg. per liter. The observation of others that sodium lactate administration abruptly decreases the plasma quinidine concentration may explain in part the dramatic improvement observed in this patient. The authors believe that acidosis was probably a factor in producing the shock-like state observed in the second patient. They were unable to obtain determinations of the blood pH in case 1. The intravenous administration of molar sodium lactate helped restore the blood pressure in both patients. The third patient with diabetic acidosis and impaired renal function, went into a shock-like state with markedly widened QRS complexes after the administrations of 600 mg. of procainamide intravenously in 6 minutes. The intravenous administration of molar sodium lactate promptly speeded up the slow rhythm and narrowed the widened QRS complexes.

The combination of molar sodium lactate and a sympathomimetic drug has been shown to increase the blood pressure to levels greater than might be expected with either agent alone. Experimental studies suggest that a priming dose of intravenously administered molar sodium lactate increases the tolerance to both quinidine and procainamide given by vein. Preliminary clinical observations suggest that molar sodium lactate may reverse the toxic electrocardiographic manifestations and the hypotension from both drugs without significantly changing the therapeutic efficacy.

Adult Chronic Bronchitis—Continuous Antibiotic Therapy. G. Edwards and E. C. Fear. Brit. M. J. 2:1010-1012 (Oct. 25) 1958 [London].

The authors report the results of an 18-month follow-up study of 42 patients with chronic bronchitis, 29 of whom were treated with oxytetracycline and 13 were treated with a sulfonamide preparation and autogenous Hemophilus influenzae vaccine. Continuous and prolonged treatment with oxytetracycline for one year or more not only prevented relapse in patients with chronic bronchitis but increased the rate of improvement the longer the therapy was maintained. The relapse rate in the group of patients not receiving oxytetracycline was considerably greater than in those treated with this antibiotic; less patients in the group not receiving oxytetracycline were improved and some became worse. Acute exacerbations of chronic bronchitis assume major proportions during the fall and winter, particularly between September and February, when 80% of the relapses tend to occur. It is suggested that continuous therapy with oxytetracycline for one period of about six months in each year, to include the period of maximum relapse, may prevent exacerbations and maintain most patients with bronchitis in effective and useful employment.

Asiatic Influenza in a Midwestern Town: With a Comparison of Intradermal and Subcutaneous Vaccination. L. J. Kirkham. J. Iowa M. Soc. 48:593-598 (Nov.) 1958 [Des Moines].

In order to investigate the relative effectiveness of intradermally and subcutaneously injected influenza vaccine the author studied the over-all incidence of influenza in the town of Mason City, Iowa, during the epidemic of November, 1957. Ninety-three (44.1%) of 211 persons selected at random who had not received influenza vaccine contracted influenza during the epidemic. Two hundred fifty questionnaires regarding the 2 techniques of vaccination were sent out to selected persons who had medical reasons for avoiding influenza and who had consequently been vaccinated. One hundred ninety-eight usable replies were received. Of these 74 had been given 0.1 cc. (20 CCA [chicken cell agglutination] units) intradermally, and 37 had been given 0.1-cc. intradermal injections with a week's interval between them. Thirty-one persons had been given 1.0 cc. (200 CCA units) subcutaneously and 54 had been given 0.1-cc. intradermal injections and an additional 0.9 cc. subcutaneously because no reaction had occurred after intradermal injections.

There was no significant difference in the protection afforded these persons. About 10% of all vaccinated individuals contracted influenza regardless of the size of the dose and the method used in administration. The incidence of influenza of about 45% in the general population compared to 10% incidence of influenza in the vaccinated population indicates that the vaccine protected about 3 out of 4 individuals. Thus the vaccination was effective in about 75% of all vaccinated persons. There was no significant difference in number of days of disability between the groups who had received intradermal injections and the general population group. The illness may have been somewhat less severe and seemed to decrease the number of days of disability in those who had received the subcutaneous injections of the vaccine in a 200-CCA dose, but the number of cases was too small and the method of sampling too inaccurate to support a definite conclusion. The disease had a decidedly adverse effect on life expectancy in those persons who were past the age of 60 years. It is therefore suggested that physicians immunize such patients as rapidly as possible, since the occurrence of this particular strain of type A influenza virus is to be expected throughout the next 10 years.

Influenza Encephalitis. S.-I. Oftedal. Tidsskr. norske lægefor. 78:996-998 (Oct. 15) 1958 (In Norwegian) [Oslo].

In Vestfold Central Hospital a number of milder complications from the central nervous system were seen in connection with Asian influenza. The history of the disease was typical—sudden high temperature, slight catarrhal symptoms, pain in muscles and joints, and general indisposition. Several cases occurred simultaneously. The 4 cases where antibodies against the influenza virus of Asian type were demonstrated in the serum are reported in detail. The complications appeared from a couple of days to 2 weeks after the onset of Asian influenza. The psychic complications all presented the same pattern but in different degree. There were symptoms of somnolence, disturbance in consciousness, paranoid delusions and hallucinations, not, however, the insomnia and restlessness at night described in lethargic encephalitis. The psychic phenomena lasted for from 1 week to 6 or 7 weeks. The electrocardiographic changes were fairly parallel with the clinical symptoms, but usually continued somewhat longer. The slight increase in cell count and albumin found in the 2 patients in whom the spinal fluid was examined in the acute phase disappeared on regression of the clinical symptoms. The cases of encephalitis were comparatively light, with complete recovery. The psychic symptoms seemed most marked in the patients who before the start of the illness had shown signs of psychic disturbance.

Role of Hemolysis in Anemia Secondary to Chronic Lymphocytic Leukemia and Certain Malignant Lymphomas. J. G. Freymann, S. B. Burrell and E. A. Marler. New England J. Med. 259:847-855 (Oct. 30) 1958 [Boston].

The authors studied the hemolytic rates and erythropoiesis in 8 men and 9 women between the ages of 33 and 77 years, with chronic lymphocytic leukemia or malignant lymphoma of the lymphocytic or follicular types. All but 1 had negative reactions of the blood to the Coombs' test. There was minimal or no shortening of the erythrocyte life span, as determined by radioactive sodium chromate (Cr^{51}) tagging, in 9 of 10 patients whose hemoglobin levels did not fall below 7.5 Gm. per 100 cc. There was a linear decrease in erythrocyte life span as the anemia increased in severity (below 7.5 Gm. per 100 cc. of hemoglobin). Splenic sequestration of tagged erythrocytes occurred in the latter group, but not in the patients with near normal biological half life of radioactive chromate ($T\frac{1}{2}$ Cr^{51}), even when splenomegaly was massive. There was no correlation between the size of the spleen and the degree of erythrocyte sequestration.

Reticulocytosis and bone marrow erythropoiesis were strikingly decreased in patients with negative Coombs' tests, even those with the most severe hemolysis. This was in contrast with 5 other patients (2 men and 3 women) with chronic lymphocytic leukemia whose age range corresponded with that of the 17 patients and who had similar degrees of anemia but had positive reactions to the Coombs test. These 5 patients had marked evidence of healthy bone-marrow response. Thus, the equal degrees of anemia found in the 2 groups of patients had probably been reached by different means. In the group with positive Coombs' tests a highly active erythropoietic system was unable to keep up with even more active hemolysis. In the group with negative tests there was slower hemolysis but little, if any, ability on the part of the marrow to compensate for it. It is believed that inadequate erythropoiesis was a major cause of anemia in all the patients with negative Coombs' tests and that occult hemolysis became of importance only as the hemoglobin level fell progressively below 8 Gm. per 100 cc. Most of the patients had received roentgenotherapy to the spleen or treatment with alkylating agents before their hematological states were studied. Alkylating agents, particularly chlorambucil [p-(di-2-chloroethyl) aminophenylbutyric acid] apparently precipitated sudden hemolysis in some patients who, although anemic, had been relatively stable before therapy.

Paroxysmal Nocturnal Hemoglobinuria: A Case Report with a Negative Ham Presumptive Test Associated with Serum Properdin Deficiency. R. K. Blaisdell, R. E. Priest and E. Beutler. Blood 13: 1074-1084 (Nov.) 1958 [New York].

The authors report on a 51-year-old Negro woman who for years had had periodic weakness and vague abdominal discomfort. She admitted passing dark urine occasionally but this did not seem to bear any relationship to the attacks of weakness, to abdominal pain or to sleep. The weakness progressed in severity with dyspnea on exertion, palpitation, and swelling of the ankles. Ham's presumptive test for paroxysmal nocturnal hemoglobinuria was performed with negative result, accounting for the failure to make the correct diagnosis initially. With the discovery of hemosiderinuria, Ham's complete acid hemolysis test was performed and gave atypical results in that there was no hemolysis when the patient's red blood cells were incubated with her serum, with or without acidification. The patient's acidified serum also was incapable to hemolyze the red blood cells from another patient with established paroxysmal nocturnal hemoglobinuria. Special studies of the patient's serum revealed a deficiency of properdin, while magnesium and complement did not appear to be lacking. It is suggested that the false-negative presumptive test for paroxysmal nocturnal hemoglobinuria and the atypical results of the complete acid hemolysis test for this condition are due to a loss of the in vitro hemolytic activity of the serum associated with a deficiency of properdin.

Additional tests showed that there was acidosis associated with renal insufficiency. This acidosis did not appear to accelerate the hemolytic process, for there was no apparent reduction of hemolytic activity in vivo when the acidosis was corrected by the administration of sodium bicarbonate. There was a progressive decline in circulating hemoglobin to 5.2 Gm. per 100 cc. and the alkalization program, therefore, was abandoned after 67 days. The patient was given transfusions, initially of whole blood and subsequently of washed blood cells. With each rise in circulating hemoglobin there was amelioration of symptoms, but these periods of improvement were brief. Acute, severe abdominal pain with distention supervened. Despite the transfusions with washed blood cells, antimicrobial drug therapy, and digitalization, the patient died. Autopsy revealed an acute generalized fibrinopurulent peritonitis as the proximate cause of death; the pathogenesis of this peritonitis was not apparent. Other findings suggested that the protracted deposition of massive quantities of iron in the kidney may play a role in the not uncommon occurrence of renal disease in patients with paroxysmal nocturnal hemoglobinuria.

Idiopathic Hypercalcuria. P. H. Henneman, P. H. Benedict, A. P. Forbes and H. R. Dudley. New England J. Med. 259:802-807 (Oct. 23) 1958 [Boston].

There are many causes of hypercalcuria: hyperparathyroidism; osteoporosis, while the disease is progressing; Cushing's syndrome and high-dosage ACTH and corticoid therapy; high intake of calcium and administration of vitamin D; sarcoidosis and beryllium poisoning; osteomalacia of renal origin, such as renal tubular acidosis; hyperthyroidism; metastatic cancer; multiple myeloma; and so forth. In this paper a condition is described in which the cause of the hypercalcuria is not clear—hence, the term "idiopathic hypercalcuria." This syndrome, which is illustrated by 35 male patients, is characterized by a normal serum calcium level, a low serum phosphorus level, and an increased urinary calcium excretion. This dislocation of homeostasis has been brought to the attention of the authors in the kidney stone clinic because of associated kidney stones.

These 35 patients are compared with 14 patients with mild hyperparathyroidism. Both groups had equally elevated urinary calcium levels and equally depressed serum phosphorus levels; the group with idiopathic hypercalcuria had normal serum calcium levels whereas the hyperparathyroid group had hypercalcemia. The kidney stones formed in the group with idiopathic hypercalcuria were characteristically composed of calcium phosphate and calcium oxalate and without magnesium and ammonium phosphate; this composition suggests that the stones were formed while the patient was in a state of hypercalcuria without an abnormally alkaline urine. Balance studies demonstrate increased calcium absorption in 4 patients. Sodium phytate decreases the hypercalcuria in this syndrome and prevents stone growth and recurrence.

Epidemic Hemorrhagic Fever Attack Rates Among United Nations Troops During the Korean War. J. R. Paul and W. W. McClure. Am. J. Hyg. 68:126-139 (Sept.) 1958 [Baltimore].

In spite of extensive investigations during the past 5 or 6 years, identification of the etiological agent of the type of hemorrhagic fever encountered among United Nations troops in Korea during the Korean war (1950-1953) and its mode of spread are still considered unfinished problems. One segment of the investigations has been concerned with the prevalence of this disease in various parts of Korea. Attempts were made to measure differential rates at which UN troops acquired hemorrhagic fever in different geographical areas during and just after the last 2 years of the Korean war and particularly during its last few months, i. e., the spring of 1953. The object of these studies was to relate high and low prevalence with local character of the terrain. In line with the suggestions made by others, the authors believe that the season exerts a considerable influence upon the epidemiology of the type of hemorrhagic fever encountered and that the terrain and local environment experienced by troops both during combat and the months immediately afterward also played a part. Under the conditions of the surveys, in which differential attack rates were measured, hemorrhagic fever seemed to flourish better in the spring and the autumn among military personnel who were living in tents or bunkers in the midst of rural or semiwild surroundings and overgrown fields, usually on abandoned farms, than among troops in areas which were mountainous and heavily forested. This does not necessarily imply that the etiological agent of hemorrhagic fever was limited to the special terrain but that conditions were such that they may have increased exposure within certain areas.

Folic Acid Deficiency and the Megaloblastic Anaemias. I. Chanarin and B. B. Anderson. Proc. Roy. Soc. Med. 51:757-763 (Sept.) 1958 [London].

Megaloblastic anemia is the consequence of deficiency or interference with utilization of vitamin B_{12} or folic acid. The etiology of those megaloblastic anemias which respond completely to treatment with vitamin B_{12} is simple: They are due to a deficiency of vitamin B_{12}, and this is almost invariably due to a failure of absorption of this factor, rarely to an inadequate dietary intake. The megaloblastic anemias which the authors discuss do not respond adequately to vitamin B_{12}, and folic acid is required in their treatment. A table lists idiopathic steatorrhea, pregnancy, anticonvulsant treatment of epilepsy, leukemia, cirrhosis, tropical sprue, nutritional megaloblastic anemia, and kwashiorkor as the conditions with which these megaloblastic anemias are associated. Megaloblastic anemia requiring folic acid treatment is far more common in tropical and semitrophical countries than in the temperate zone. The condition may be due to malabsorption, increased demand, impaired utilization, or reduced intake of folic acid and to such factors as an abnormal intestinal flora.

Methods are described which are concerned with the assessment of folic acid deficiency and with the measurement of folic acid absorption. These techniques are reviewed in relation to the various types of megaloblastic anemia. Impaired utilization may be due to folic acid antagonists, such as Aminopterin and Amethopterin, and also to the anticonvulsant drugs used in the treatment of epilepsy. Impaired utilization may also result from a primary vitamin B_{12} deficiency. The role of bacteria in producing megaloblastic anemia is uncertain. They may interfere with the absorption of folic acid, as in tropical sprue, and with the absorption of vitamin B_{12}, as in patients with anatomic lesions of the small intestine. Whether these bacteria can also produce substances which act as folic acid antagonists has not been demonstrated.

Hypogammaglobulinemia (Agammaglobulinemia) in a Ten-Year-Old Girl. W. H. Civin and D. H. Sandberg. Hawaii M. J. 18:35-38 (Sept.-Oct.) 1958 [Honolulu].

A 10-year-old Japanese-Caucasian girl was repeatedly admitted to the hospital with bouts of infection. Three separate electrophoretic studies revealed no gamma globulins, and no cause for the absence of this serum globulin fraction could be elicited. The patient was treated with antibiotics, gamma globulin, and transfusions. Despite improvement, infections continued to occur, and the patient died during the 9th hospital admission in 6 years. Autopsy revealed numerous abscesses containing Proteus vulgaris, and there was one abscess in the cerebrum containing a branched acid-fast organism which either belonged to the Nocardia genus or was Mycobacterium tuberculosis.

Agammaglobulinemia has been reported with hypoproteinemia, lymphoma, and thymona. It has also been reported without apparent cause, in which case it may be either congenital or acquired. Gamma globulins are not synonymous with antibodies, and an elevated level of gamma globulins may be associated with absence of antibodies, as in multiple myeloma. Other mechanisms for combating infection occur in the absence of antibodies which migrate with the gamma globulin fraction. Laboratory methods of diagnosis of agammaglobulinemia deal with the determination of gamma globulins or of antibodies, and the two are not synonymous in the laboratory any more than they are identical in effect clinically. The case discussed is one of acquired agammaglobulinemia. Both its history and the discussion point up the defects in our knowledge concerning natural resistance to infection.

PUBLIC HEALTH

The Epidemiology of Psittacosis and Report of a Turkey-Borne Outbreak. R. D. Leachman and E. M. Yow. A. M. A. Arch. Int. Med. 102:537-543 (Oct.) 1958 [Chicago].

On Aug. 28, 1956, about 2,500 turkeys were brought to Houston from a farm 11 miles north of Waller, Texas. The birds were processed by 2 poultry plants before Sept. 1. The week after delivery a febrile illness began to appear among workers in the 2 processing plants. Twenty of the 41 employees of plant A had symptoms indicative of psittacosis, and a rising titer of complement-fixing antibodies was found in 13. Most of these patients improved promptly after the institution of tetracycline therapy. One patient who did not seek medical aid until the symptoms had been present for a week died 5 days later, despite intensive antibiotic therapy. There was no psittacosis among the office workers, who had no direct contact with the turkeys. The group with the highest attack rate worked in the unloading and picking areas, where fluttering of wings stirred dust from the droppings and feathers. The patient who died was employed in this area; in addition, he was janitor for the plant and killed the birds. There were 40 employees in plant B. Although these persons were not studied as thoroughly as those in plant A, there were 11 with clinical symptoms of psittacosis and with positive complement-fixation tests.

Apparently some of the turkeys had not appeared normal at the time of shipping, and, when the flock was inspected, many of the remaining 1,500 birds in the older group had become sick and some had died. The pathological examination of the sick turkeys revealed evidence of ornithosis, and the virus causing this disease was isolated from them. Visable psittacosis virus was also found in the carcasses which had been sent to the Texas Department of Public Health laboratories. It was concluded that turkeys were the source of the human infection in the Houston poultry processing plants. Of the birds remaining at the farm, all were subsequently treated with tetracycline and were ultimately cleared of the infection. The history of the epidemiology of psittacosis is reviewed.

BOOK REVIEWS

Callander's Surgical Anatomy. By Barry J. Anson, M.A., Ph.D., Chairman, Department of Anatomy and Robert Laughlin Rea Professor, Northwestern University Medical School, Chicago, and Walter G. Maddock, M.S., M.D., F.A.C.S., Edward S. Elcock Professor of Surgery, Northwestern University Medical School. Fourth edition. Cloth. $21. Pp. 1157, with 1047 illustrations. W. B. Saunders Company, 218 W. Washington Sq., Philadelphia 5; 7 Grape St., Shaftesbury Ave., London, W. C. 2, England, 1958.

As stated in the preface to this new edition, this highly successful volume has been modified only to the extent of bringing up to date technical procedures in surgery and new knowledge in the field of anatomy. The format of the book is essentially the same as in the preceding editions, but it is about 100 pages longer and has about 100 more illustrations. The factual material continues to be accurate, and the form of presentation is useful not only from the point of view of reference to a particular detail but also to the field as a whole. This will probably remain a standard textbook for use in courses in surgical anatomy for medical students and will continue to be a useful reference for anatomic review for the surgical resident and the busy surgeon. It continues to correlate applied anatomy and surgery in a readable yet precise manner. The surgical aspect of the book concerns rationale rather than detailed technical description or instruction. Of particular value are the figures presenting anatomic variations in areas of importance to the surgeon. This feature alone would justify its inclusion in the surgeon's library. A number of the most recent developments in surgery have not been included. Some of the developments in vascular surgery, particularly, are perhaps too briefly mentioned. Except for its use as a textbook in courses in surgical anatomy, this volume must continue to serve as a supplement to more complete works on human anatomy.

The Management of Emergencies in Thoracic Surgery. By John Borrie, M.B.E., Ch.M., F.R.C.S., Thoracic Surgeon, Dunedin Hospital and Southern Metropolitan Region, Dunedin, New Zealand. Foreword by Sir Russell Brock. Cloth. $10. Pp. 340, with 300 illustrations. Appleton-Century-Crofts, Inc., 35 W. 32nd St., New York 1, 1958.

This is an excellent monograph on emergencies in thoracic surgery. As a reference book, it should be of service to specialists in thoracic surgery, but its chief appeal should be to the general practitioner and the general surgeon who are usually the first ones to be confronted with these emergencies. It is important that they be familiar with this field and that they be capable not only of recognizing the emergency but also of instituting the required treatment. This book should be in the emergency room of every hospital and in the library of every physician.

Handbook of Respiration. Analysis and compilation by Philip L. Altman, John F. Gibson, Jr., M.D., and Charles C. Wang. Edited by Dorothy S. Dittmer and Rudolph M. Grebe. Prepared under direction of Committee on Handbook of Biological Data, Division of Biology and Agriculture, National Academy of Sciences, National Research Council. Paper. $7.50. Pp. 403, with illustrations. W. B. Saunders Company, 218 W. Washington Sq., Philadelphia 5; 7 Grape St., Shaftesbury Ave., London, W. C. 2, England, 1958.

A stupendous amount of quantitative information about the mechanical and chemical aspects of respiration is made available by this remarkable volume. It is the sixth in a series of compilations of numerical data, mostly in tabular form, from various fields of biological science. Previous volumes have been devoted to hematology, nutrition and metabolism, toxicology, and general biological data. The data in the present volume are collected under 14 headings: basic physical and chemical data, basic respiratory anatomy, lung volumes and pulmonary function, blood respiratory characteristics, erythrocytes and respiratory pigments (including pyrrole pigments and cytochromes), mechanics of breathing, artificial respiration, effects of exercise, effects of inhaled gases, effects of ionizing radiations and other disturbing factors, oxygen consumption, tissue respiration in animals, and the same in plants. Since most of the data have meaning only in terms of the methods by which they were obtained, the bibliographic references are an essential feature of the book. Moreover, the problem of tabulating results obtained by different investigators under the most varied conditions can be solved only by securing the collaboration of reviewers who are able to criticize and assimilate the material. This work has been well done, and the book testifies to a magnificent spirit of cooperation among the editorial committee, the handbook staff, and the long list of contributors and reviewers. It should be represented in every library used by persons doing research in the medical sciences.

These book reviews have been prepared by competent authorities but do not represent the opinions of any medical or other organization unless specifically so stated.

QUESTIONS AND ANSWERS

RABIES IMMUNIZATION

To the Editor:—*A patient, bitten by a suspected rabid animal, received a 14-day course of rabies vaccine (duck embryo). How long does the immunity last from such vaccination? If the patient were bitten by another suspected rabid animal in the future, should he receive another 14-injection series or would fewer injections suffice, due to a "recall phenomenon"? Could the patient's serum be used as antiserum in treatment of another patient who required rabies antiserum therapy if the two bloods were compatible for ABO groups and Rh factor? If so, how much serum should be used?*

Jack E. Kaufmann, M.D., David City, Neb.

Answer.—The antibody response to a course of antirabies vaccine is measured by the neutralizing "power" of the recipient's serum when incubated with live rabies virus and later injected intracerebrally into susceptible mice. This has been done in a limited number of individuals on an experimental basis but is not a routine procedure. A recent article by Fox and co-workers (*Bull. World Health Organ.* 17:869, 1957) summarizes their observations in this respect: "Study of recipients of Pasteur treatment indicated that antibody commonly persists for at least 5 years after a single course and for 15 or more years after re-treatment. It was also observed that the ability to respond to a booster of HEP Flury vaccine persists for at least 25 years. The response elicited by the booster is prompt and is usually at least equal to that resulting from a full primary course. The suggested conclusion is that previously treated persons need not receive more than a single booster on reexposure, and that Pasteur treatment provides a solid basis for long-sustained immunity." HEP Flury vaccine is an experimental avian embryo product somewhat similar to the duck embryo vaccine, and there is reason to believe that any potent antirabies vaccine would elicit a response very similar to the one observed by Fox and co-workers. Their results were derived from studies on 136 volunteers. It may be advisable to administer two booster doses instead of the single injection to previously treated persons if the exposure for which they are receiving treatment is severe. The use of serum from a person who has undergone treatment with antirabies vaccine for prophylaxis in another exposed person would pose the difficulty of testing the potency of the serum and consequently of estimating proper dosage. Commercial antirabies immune serum (horse origin) is administered in a dose of 0.25 ml. per pound of body weight, the potency of the product being standardized to contain at least 80 international units per milliliter. In order to arrive at an equivalent dosage, the human serum would have to be tested against the international standard. It could then be used much as the commercial product is.

EGG ALLERGY AND FERTILITY

To the Editor:—*Is there any evidence that an acute allergy to eggs on the part of the husband would be a cause for infertility? Could the sperm reaching the human egg be immobilized or destroyed? A husband reacted to a scratch test for egg allergy with the entire arm becoming swollen and red. He is able to detect minute quantities of egg used in cooking by a tingling of the tongue—which protects him from ingesting egg unknowingly in breads, pie crusts, coffee, and other foods. His allergies also include chicken, hen turkey (not rooster or tom turkey), fish, and honey. A complete examination for causes of infertility gave negative results throughout. It is realized that these allergies may be an indirect cause of the infertility because of the lack of certain food factors, but could this violent reaction to egg be a direct cause? Do sperm, as body cells, carry the allergic factors with them, or are these factors present in the spermal fluid? Have there been any cases in which a husband with a strong egg allergy has fathered children?*

J. G. White, M.D., Stamford, Conn.

Answer.—The genetic factors determining allergy are carried by the human sperm cell as well as by the ovum. In neither case does this factor determine a specific allergy but, rather, a tendency to develop sensitizations of any kind. The father or mother may be allergic to egg, while the offspring may develop allergy to ragweed pollen or wheat

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The answers here published have been prepared by competent authorities. They do not, however, represent the opinions of any medical or other organization unless specifically so stated in the reply. Anonymous communications cannot be answered. Every letter must contain the writer's name and address, but these will be omitted on request.

or be entirely free of allergy. There is no evidence that acute allergy to egg, or, for that matter, allergy to any other food or inhalant, in the husband or wife is a cause of infertility. This consultant, in an experience of over 35 years, has seen many fathers and mothers with egg allergy. One speculative possibility can be considered: Experimentally, it has been possible to produce in animals an allergy to its own tissues, so that the tissue antibodies go on to damage and destroy an organ. One of the earliest demonstrations of this kind of autosensitization has been produced by Jules Freund and associates. A testicle removed from a guinea pig and a portion of the homogenized tissue reinjected in the same guinea pig produced degenerative changes in the remaining testicle with final aspermatogenesis. Autosensitization in man occurs in certain blood diseases and probably also in diseases of other organs, such as thyroid, kidney, heart, and nervous tissue. It is possible that infertility in the male may also be at times produced on this basis. This concept would entail a prior injury of the testicle (due to trauma, virus infection, drug, or other factors) followed by the production of testicular antibodies which produce final damage to the sperm-producing tissue. It can be speculated further that such an autosensitization process might be more likely to occur in persons who have other allergies. In the particular case cited, the finding of adequate and active spermatozoa would rule out such a possibility.

Answer.—A positive relationship between extremely violent food sensitivity and sterility has been noted by many observers. Though such instances are few, in almost all cases it was the wife who was allergic and in whom control of the allergy led to normal fertility. The British allergist, Dr. Vera Walker, has studied 16 such cases. It is doubtful that the spermatozoa of a human male sensitive to hen's egg would be immobilized or destroyed in the nonallergic environment into which they were placed, although they carry the genes of potential allergy. In reviewing case histories, this consultant could find no record of a married, egg-sensitive male who failed to have children. On the contrary, a number of patients extremely sensitive to common foods, including egg, have married and have brought their children and, subsequently, their grandchildren for studies concerned with food sensitivity. One sometimes wishes they were less fertile. If such allergy were a cause of infertility in only a small percentage of allergic patients, it would not be as difficult as it is to find subjects for studies linking the two states. Recent work in sterility implies that autoimmunity may be a factor (McMaster, *New York J. Med.* 58:2980, 1958).

RHEUMATIC FEVER AND HEARING LOSS

To the Editor:—*A 28-year-old woman, two months pregnant, has inactive rheumatic fever (last attack one year ago). Her husband has recovered from rheumatic fever. One of the children now has rheumatic fever, and a parent of the patient had rheumatic heart disease. Her second child, a girl, was born with nerve deafness (85% hearing loss). There is no history of syphilis or quinine therapy. Specifically, she wants to know the chances, possible causes, and prevention of hearing loss in the present fetus. Generally, is there any known etiological connection between rheumatic heart disease and hearing nerve involvement?*

Lester Lando, M.D., Monsey, N. Y.

Answer.—As far as is known, there is no relationship whatsoever between rheumatic heart disease and nerve deafness in the offspring. Therefore, chances are excellent that the present pregnancy will not result in a nerve-deaf child. It is known that German measles in the first trimester of pregnancy, as well as the Rh blood factor, may produce nerve deafness in the offspring. Likewise, certain drugs, especially quinine, have been known to have a similar effect. It is also known that some children are born with nerve deafness without any apparent cause, other than its being of congenital origin.

LEUKOCYTOSIS

To the Editor:—*A 36-year-old woman, a laboratory technician, has repeatedly shown a white blood cell count of 14,000 to 15,000 per cubic millimeter. The usual differential is 84% segmented neutrophils, 5% band cells, 7% lymphocytes, 2% monocytes, and 2% eosinophils. During two past pregnancies her white blood cell count reached 18,000 to 25,000 per cubic millimeter. The platelet count was 289,000, reticulocytes 2.3%, hemoglobin level 11.4-12.0 Gm.%, hematocrit value 38%, and corrected sedimentation rate 11 mm. per hour. After each pregnancy, the white blood cell count receded to its basal level of 14,000 to 15,000 per cubic millimeter. No adenopathy or hepatosplenomegaly is apparent. Bone marrow examination has revealed nonspecific myeloid hyperplasia rather than any appearance of early chronic granulocytic leukemia. Please discuss the implications and prognosis of this case.*

Leonard Breslaw, M.D., Los Angeles.

Answer.—With the data presented, it would be impossible to make a categorical statement. One can do no more than speculate about the implications and the prognosis. The period of observation is not known, and it may only be assumed that it has been at least three years. The findings with exacerbation in pregnancy could well be wholly normal for this person, and the likelihood is that no serious disease will be forthcoming. However, it is not specifically stated whether the patient has anything to do with x-ray equipment or radioactive substances which could have some bearing on the hematological abnormalities. Occasionally, leukocytosis may precede, as well as be associated with, polycythemia, thrombocytosis, or other myeloproliferative diseases which only the future could resolve.

ULTRASOUND AND HEADACHES

To the Editor:—*This problem concerns the evaluation of headaches and emotional irritability in a group of men working in a large aluminum plant. In one particular part of the plant, ultrasound is used to test for structural defects. A frequency of from 200 kilocycles to 25 megacycles is used. The operator of the ultrasound machine directs the passage of the transducer over the metallic member and detects any structural flaws by looking constantly at a cathode ray oscilloscope—for periods up to eight hours. The foreman and all the men under his jurisdiction have complained of chronic headaches and increased emotional irritability. They believe that the ultrasound has something to do with their symptoms. Although the men are not in direct line of the direction of the sound waves, they are required to clean the crystal covering the sound transducer and they work in an enclosure approximately 60 ft. long by 40 ft. wide. No authoritative reports have been seen which will help in determining whether the sound may be an etiological factor in producing the headaches and nervous irritability. Also, could peering at an oscilloscope screen for extended periods of time be a causative factor in the production of these headaches?*

Marvin B. Wolf, M.D., Adrian, Mich.

Answer.—This is a very interesting question. This consultant has had many similar inquiries regarding ultrasound, although the symptomatology allegedly due to ultrasound has been different in some of the cases. Present beliefs are that ultrasound will not have any untoward effect on hearing. Some difficulty has been found due to ultrasonic use as related to heat. This effect is on the local tissue, that is, through direct contact with the ultrasound by way of fluid mediums. In these cases, gloves seem to be enough protection to prevent any significant injury. The inquirer has put his finger on the problem by reference to the oscilloscope. It is true that watching a radar screen or an oscilloscope (which in effect is a radar screen) for long hours produces headaches and, as a result, nervous irritability. There is no evidence available that will support the claim that headaches and nervous irritability are due to exposure to ultrasound. Some other factor must be responsible.

ELECTROSHOCK THERAPY

To the Editor:—*A rare complication of electroshock treatment is said to be ventricular fibrillation. To what extent does succinylcholine, given intravenously in doses of 10 to 14 mg. before treatment, predispose to ventricular fibrillation? Does the use of atropine in doses of 0.6 to 1 mg. before electroshock therapy is done protect against cardiac side-effects? Are there any other methods of preventing them? What measures, medical and/or surgical, are indicated if ventricular fibrillation occurs after electroshock therapy? Does the rapidity of injection of succinylcholine have any bearing on the incidence of ventricular fibrillation?*

Edward L. Colman, M.D., Fergus Falls, Minn

Answer.—Succinylcholine chloride is considered to be the safest drug employed to reduce muscular contractions that accompany convulsive seizures in electroshock therapy. Premedication with atropine, usually 1/75 grain (0.8 mg.) is advisable for its cardiac effect. It also diminishes salivation nausea and vomiting that at times may follow electroshock therapy. Preliminary sleep is usually induced by thiopental sodium given intravenously to relieve anxiety. Oxygen may be given at the time sleep is induced and should be administered, under pressure, during the brief state of apnea which results from the effect of succinylcholine. Oxygen administration should be continued until spontaneous respiration is restored. Administration of succinylcholine renders electroshock therapy safer, as far as the heart is concerned, as it diminishes considerably the rise in systolic pressure during the treatment. Recent coronary thrombosis and cardiac failure constitute contraindications to electroshock therapy. Transient cardiac arrhythmias are not uncommon in this treatment. There is no evidence that the administration of succinylcholine predisposes to ventricular fibrillation.

Answer.—It has never been demonstrated, either experimentally in animals or in man, that alternating current of the strength and duration used for electroshock therapy can produce, when applied to the brain, fibrillation of the ventricles of a normal heart. Succinylcholine, on the other hand, has no known pharmacological effects on the cardiac mechanism or, for that matter, on the entire cardiovascular system except for a slight elevation of the blood pressure during slow administration, attributable to sympathetic ganglionic stimulation. There is, therefore, no basis for the assumption that the combined effects of these two factors may precipitate ventricular fibrillation. Atropine may prevent occurrence of certain arrhythmias commonly seen in the "vagal phase" of convulsive therapy, viz., sinus bradycardia, slow ectopic rhythms, and disorders of atrioventricular conduction. Proper management of circulatory arrest in the course of electroshock therapy depends, as in other such cardiac emergencies, on establishing as quickly as possible the type of abnormal mechanism, whether rapid ectopic impulse formation or cardiac standstill. Such a distinction is greatly aided by the monitoring of cardiac events on a cardioscope, which should be part of the routine equipment in any set-up for shock therapy. In this way, the critical four-minute period during which resuscitation is feasible can be utilized for immediate rational procedures (pounding of the chest, needling of the heart, intracardiac injection of a sympathomimetic drug, application of an external artificial pacemaker, or quick opening of the chest for rhythmic manual compression of the ventricles for intracoronary injection of appropriate drugs or for direct application of electric shocks).

PURITY OF DRINKING WATER

To the Editor:—*A water system in a Rocky Mountain area is constructed, essentially, in the following manner: A system of large and small collecting reservoirs, approximately 30 to 140 miles from a large city, feed over rapid, downhill streams into settling reservoirs which in turn feed into filter plants for the city drinking water supply. The present sanitation board, which claims the backing of the state health department, has maintained that the outlying collecting reservoirs, if used for recreation, i. e., boat fishing, would constitute a health hazard by reasons of drownings, illegal bathing, or other illegal human contact with the water. An opinion is desired as to the health aspects of the use of these outlying collecting basins (but not the settling basins) for fishing only in the face of the history of their use in other areas of the United States.*

M.D., Colorado.

Answer.—The purity of a city drinking water supply will depend on the degree of contamination of the outlying collecting reservoirs. Utilization of the areas around such reservoirs for recreation or fishing does represent a risk of contamination of the water. It is certainly true that fishing is allowed in the collecting reservoirs of many municipal areas. The question of fishing privileges is answered, in individual areas, after several factors are taken into consideration. Some of these factors involved are the purity of the water prior to the use of these areas for fishing, the amount of fishing allowed, the total volume of the reservoir and its turnover rate, and the efficiency of the water purification system. The use of such areas for fishing represents a health risk, but it may be extremely small.

INFECTIOUS MONONUCLEOSIS

To the Editor:—*Please comment on the allegation that a person with blood type A who has infectious mononucleosis would have a negative Paul-Bunnell reaction, i. e., that non-Forssman type of antibodies would not be demonstrated by the sheep red blood cells or differential reactions in the blood.*

N. R. Bouziane, M.D., Montreal, Canada.

Answer.—Persons of blood group A who have infectious mononucleosis have a positive Paul-Bunnell reaction, the same as persons of any other blood group. Also, the differential reactions for infectious mononucleosis are not influenced by the blood group of the patient. The statement in the query is not clear, unless it is meant that the Forssman type of antigen in red blood cells of group A would not permit the presence of Forssman type of sheep antiagglutinins in the serum. Actually, red blood cells of group A contain an antigen related to but not identical with Forssman's antigen. Furthermore, sheep red blood cells contain at least three different antigens: Forssman antigen, sheep species-specific antigen, and the specific infectious mononucleosis antigen.

PROGESTERONE FOR OVARIAN CYSTS

To the Editor:—*In regard to the answer of the consultant on the use of progesterone in the treatment of ovarian cysts, which appeared in* The Journal, *Nov. 1, 1958, page 1294, I think clarification is necessary. The consultant states, "If the etiology of the small painful cysts of the ovary is endometriosis, the administration of progesterone should aggravate, rather than improve, the condition." This statement should be amended to read "intermittent administration of progesterone," since, when progestins are given constantly and in increasing dosage for periods of five to seven months, amelioration of pain, amenorrhea, and regression in the size of ovarian enlargement have been noted in patients with proved endometriosis. I agree that the intermittent use of the progestins with subsequent bleeding from a secretory endometrium will result in increased dysmenorrhea.*

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ROLE OF PEDIATRICIAN IN PHYSICAL FITNESS OF YOUTH

W. Kenneth Lane, M.D., New York

BY THE USE of the term "pediatrician" in the title of my paper I mean to refer not only to those with specialty training in the care of infants and children but to all physicians who care for children. The pediatrician is the first friend an infant has, apart, of course, from his parents. And since parents turn to the physician for guidance in raising a healthy baby and when sickness strikes, one could say that a pediatrician is the family's best friend. The pediatrician is the first to meet the family medically and to introduce good health routines. He is the first to schedule and interpret the series of immunizations that start today in infancy and play an increasingly important role in getting the baby safely up to and through the health hazards of childhood.

A comparison of American with European school children as to physical fitness was made in 1953 by applying the six basic Kraus-Weber tests to 4,458 children in this country and about 3,000 children in Italy and Austria. These tests evaluate the strength of the psoas, the lower abdominal muscles, and the lower and upper back muscles, as well as flexibility of the back. The results showed the physical inferiority of American children in physical performance, and subsequent findings indicate that the fitness level of the general public has been falling steadily even while the performance of selected star athletes has improved. The tendency has been for the number of active participants in athletics to decrease while the number of people watching by television and applauding comfortably from armchairs has increased. The pediatrician can do much to remedy this, for he is the family's best friend. He should help the child realize early in life that a flexible, strong body is vitally important.

The pediatrician with a knowing heart can wield a lifelong influence on the healthy development of the child. He can and should contribute to family understanding of the needs of the infant, and shape his growth as he progresses into childhood and on toward adulthood. Basic health principles established early guide an individual's growth and development. Our society gives the pediatrician a chance to apply the modern concept of total care. The pediatrician is the first to recognize the well baby as an entity, and he understands that physical fitness is closely related to the mental and emotional development of the child entrusted to his guidance. Not only does physical fitness represent an important segment of child development but it increases in significance as the child progresses on to maturity.

Consultant, Respiratory and Rehabilitation Center Services, The National Foundation.

Read before the Section on Physical Medicine at the 107th Annual Meeting of the American Medical Association, San Francisco, June 26, 1958.

As we look about us today, mindful of how seriously we took our responsibilities, many of us find cause for more amazement than pride in some of the children we remember as our healthy infant patients. Too often we see deterioration instead of development, young bodies, once firm and flexible, beginning to go slack and soft. We hear about too many backaches, and we are appalled. What has gone wrong? We realize, sometimes too late, that physical fitness is not a static condition. It can be established by simple, repeated routines but those routines must be expanded and maintained.

Comparative Fitness Tests

In 1953, health leaders and school authorities were shocked into active concern about the comparative physical development of American and European children.[2] Most pediatricians may recall the facts if not the specific data. Six fairly simple, basic tests of physical fitness were given to 4,458 normal American school children. Known as Kraus-Weber tests, these included tests for abdominal muscles, lower back muscles, upper back muscles, and flexibility of back and hamstrings.[3] Similar tests were given to about 3,000 European school children, primarily in Italy and Austria.[4] At every age, from 6 to 16, the American group proved less muscular than the European group; 57.8% of the American children failed to pass, compared with less than 8.17% of the Europeans.

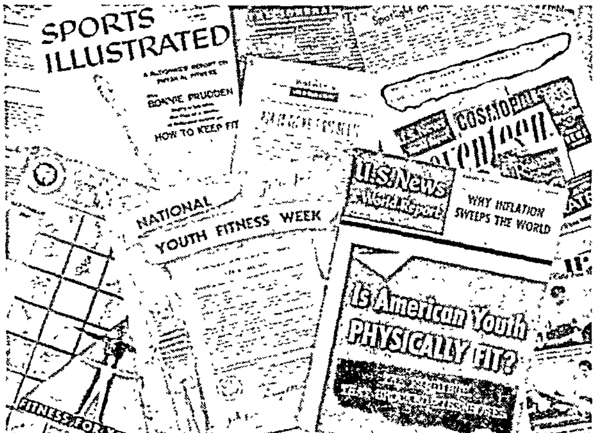

Fig. 1.—Montage of part of large number of articles appearing in press on physical fitness of youth.

Results of these Kraus-Weber tests came as a shock to most Americans, who take their physical superiority somewhat for granted, particularly in the field of sports. The President appointed a special committee to "investigate." A rash of newspaper and magazine articles analyzed, deplored, and questioned the situation (fig. 1). Were we becoming a nation of "push button softies?" Were our high standards of living responsible for the physical deterioration of our youth?

There was reason for the agitation, and there is still a point behind the questions. In March, 1958, the President's Council on Youth Fitness again was charged with alerting the nation to the potential danger toward which many symptoms increasingly point. Many who have followed these special conferences have been disappointed at the lack of concrete action by these gatherings of large numbers of highly talented people.

European children do not have the benefits of our highly mechanized society, and this seems to underscore the major difference between the physical fitness of the two groups studied. They walk where we ride. They do not use—to the extent we do—cars, school buses, elevators, or other of our great laborsaving devices. Their recreation is largely based on the active use of their own bodies; they are sports participants, where we are sports spectators. Their daily routine of living keeps them more active physically than does ours, and this activity builds muscles, develops strength, insures flexibility and fitness. We live better, eat better, have better medical care, and have more time for rest and leisure, but are these really the blessings they appear to be?

Since 1953, when these studies were first called to national attention, the situation on the American scene seems to have become worse rather than better. Television has taken tighter hold on both children and adults. In too many homes the greatest physical activity seems to consist in switching channels or moving from the television set to the kitchen to pick up a snack during commercials. Lack of physical activity has become an increased menace to the health and development of our youth.

A few years ago the following statement appeared in a report of the National Conference on Physical Education for Children of Elementary School Age: "Every child needs sufficient muscular strength to maintain good posture at rest and in motion and to do with vigorous physical activity. Strength coupled with a flexible body gives him ability to move quickly and effectively. He needs the stamina and endurance that depend on well developed heart and lungs to persist in work and play without undue fatigue. Strength, agility and endurance come from play that is long and intense enough to tax the body beyond the ordinary."[5]

The Lankenau Hospital in Philadelphia held a research conference on "Maturing Man: Growth and Aging" on Oct. 24, 1957. Kaare Rodahl, director of clinical research at the hospital, emphasized the role of physical fitness in longevity: "What a man is able to do at 70 years of age depends largely on what he did at 7."

Pediatricians should evidence greater interest in these two significant statements than they have shown to date. Very often, it is true, the pediatrician is so busy with problems of acute illness and today's numerous immunization procedures that he may overlook the necessity of encouraging patients to maintain even minimum standards of muscular fitness, but it is early interest in physical fitness that stimulates a child's desire to develop muscular strength, agility, and flexibility. If his interest lags, the child can all too easily and quickly drop below the minimum standard of fitness required for general good health and well-being. We've all seen it happen too often. Seeking medical means to alleviate muscular pains and backaches, we have found their origin not in orthopedic difficulties but in lack of sufficient exercise.[10]

Morris and Heady[6] and other English authorities,[7] as well as Benton and Rusk,[8] point to a definite relation between physical activity and coronary heart disease in middle age by reviewing employment data on cardiac cases. They have found that the disease is not so severe in physically active workers, who tend more to develop angina pectoris and other relatively benign forms, and have lower mortality. Pomeroy and White, in their study of former Harvard football players, found that those who maintained some degree of regular exercise were less prone to develop coronary heart disease and that "no individual in [their] study who maintained a heavy exercise program happened to develop coronary heart disease."[9]

Exercise and Deficiency

Developing the tests for physical fitness that bear his name, Dr. Hans Kraus [10] demonstrated that lack of sufficient exercise blocks off emotional release and decreases muscle strength. City traffic, shrill telephones, and high pressure work combine to keep us in a state of irritation but deny us the necessary physical outlet of release. Impulses inhibited from responding to such outside stimuli can, and do, result in general and local muscle tension. Physical activity, walking, and even stair-climbing, dancing, and other active sports are excellent outlets for these impulses.

There has been criticism of the Kraus-Weber tests from many sources. I do not mean to imply they are the only tests. Certainly some of the more complete physical profiles, such as those designed by the American Association for Health, Physical Education, and Recreation, give a more complete picture of total physical abilities. Almost every school of physical education has its own modification. All these are fine, but they cannot be done in a doctor's office. Kraus never implied that if a child passed his test he was *de facto* free of any medical or surgical impairment, merely that these were simple tests which had been given to large groups of children. Considerable data are available on the results. Failure in one or more of the tests indicates a lack of the minimum strength and flexibility necessary for ordinary living. These tests can be given in an office by a nurse after a short period of explanation. From a medical standpoint they are ideal, because the possibility of producing harm by the tests themselves, even before a physical evaluation, is nil.

Our mechanized, over-convenient life, by reducing muscular activities to a bare minimum, deprives us of the exercise that is necessary to maintain adequate physical fitness. Most of us get along with minimal muscular equipment until such time as a trivial occurrence forces us to exceed the existing limitations of our muscles. When we lift a 30-lb. suitcase, for instance, or stoop to pick up a dropped pencil, the effort may result in acute muscle strain which either improves by itself or causes us to seek some palliative remedy. This strain further reduces the efficiency of our muscles and we go along rather carefully until another strain occurs. Repeated episodes may lead to conditions that actually do stimulate orthopedic difficulties, and prolonged suffering frequently ties in with some emotional instability until finally we are confronted with a well-established illness that comprises not only the physical but also the emotional life of a person.[7]

Kraus showed that systematic muscle training relieves the situation. Patients encouraged to exercise improved rapidly and regained strength and flexibility, but they quickly lost ground if physical activities were reduced or given up. It is his contention that lack of sufficient exercise constitutes a serious deficiency, comparable to vitamin deficiency.

Prevention of this muscular deficiency is, it seems to me, the pediatrician's business. He cannot do it alone, of course, but he can and should play a bigger role in the basic health picture than he does now. His influence on parents, teachers, and others charged with responsibility for children's health can make a sizable dent in the growing problem. At the risk of sounding old-fashioned, I would like to remind you that physical activity was an earnest recommendation, even a prescription, of physicians in past decades. And I would like to suggest that it would not hurt us to borrow from the past and restore physical activity to its proper place of importance in a well-balanced life.

The past relates closely to the present when we review the results of the Kraus-Weber tests. A large number of children originally unable to pass the tests made the grade easily after they resumed regular exercise. Their strength and flexibility increased and their complaints lessened or disappeared, but they lost ground again if their physical activities were reduced or discontinued. This indicates rather obviously that muscle fitness levels can be controlled by exercise. It was noted that more American than European children complained of backache, but it was the effort to determine the source of the loss of flexibility and muscular strength that brought about the comparative study of school children here and abroad.

Of interest is the experience in a parochial school in Scarsdale, N. Y. When 385 children in grades 1 to 8 were tested, 59% of them failed two or more of the tests. For the next six weeks the following program was put in effect: a three-minute drill, three times a day, led by one of the students, and a 30-minute period one day a week of strenuous calisthenics led by one of the mothers. The percentage of failures dropped to 35. This program has been expanded; there are now 10 volunteer mothers giving the program, which includes basic tumbling. This is given in the school cafeteria and the chapel, in a school which has no facilities for a physical-education program.[11]

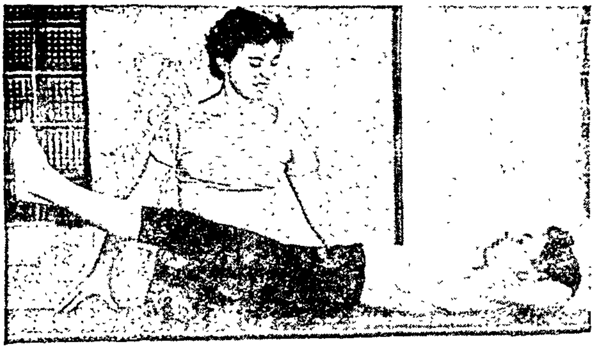

Fig. 2.—Test of strength of psoas and lower abdominal muscles.

The Kraus-Weber Tests

Many pediatricians are familiar with these six simple tests. They can easily be included during routine examinations of a patient. After a short period of instruction they could be given or supervised by the nurse. These tests represent basic minimum standards of physical fitness. They were designed to indicate the level of strength and flexibility in certain key muscular groups below which function of the whole body as a healthy organism might be jeopardized. Children whose physical fitness level falls below these minimums should be considered "sick people." They are almost invariably youngsters who bear all the earmarks of stress and who frequently manifest signs of emotional instability.

Tests of Psoas and Lower Abdominal Muscles.—In the first test of the strength of the psoas and lower abdominal muscles (fig. 2), the person being tested is supine, with hands behind neck and legs extended. Instructions are as follows: "Keep your knees straight and lift your feet 10 in. off the table. Keep them there while I count." The count is 10 seconds. If the person tested has not understood your command, he may try to raise his chest when he raises his feet and will need further explanation. Watch for an extremely arched back which may indicate weak abdominal muscles or postural habits contributing to sway back or lordosis. Holding for 10 full seconds is passing and is marked as "10." Anything less is recorded as that part of the 10 seconds that was held, for example, "4" for 4 seconds or "7" for 7 seconds.

In the second test (fig. 3), the person being tested is supine, with hands behind neck. His feet are held down on the table by the examiner. He is instructed as follows: "Keep your hands behind your neck and try to roll up into a sitting position." If the person being tested is unable to perform this movement at first try, it may be because he did not understand the directions. Help him a little and then let him try again. Watch for a "stiff back sit-up." This may indicate that either he has not understood you and needs further explanation with emphasis on "rolling up" or that he has very poor abdominal muscles and is doing most of the work with his psoas. Marking is the same as for the first test.

In the third test (fig. 4), the person being tested is supine, with hands behind neck and knees bent. His feet are held down on the table by the examiner. He is instructed as follows: "Keep your hands behind your neck and try to roll up into a sitting position." The precautions are the same as for the second test, but, as this test is usually more difficult, the tendency toward "stiff back sit-up" will be even more pronounced, and to it is added the tendency to help with one or the other elbows. Marking is exactly the same as for the first two tests.

Tests of Upper Back Muscles.—The next three tests concern the back muscles. In the first test (fig. 5), the person being tested is prone, with a pillow under his abdomen so as to give the body the feeling of being a seesaw, which if weighted at either end would be able to hold the other end in the air. This is most easily accomplished with the following instructions: "Roll over onto your stomach and lift up the middle so that I can slide this pillow under you." (Be sure the pillow is large enough to support him.) "Now, I am going to hold down your feet while you put your hands behind

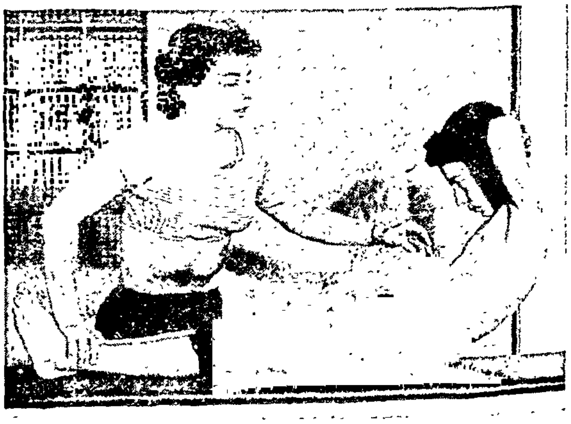

Fig. 3.—Test of strength of abdominal and psoas muscles.

your neck and raise up your chest, head, and shoulders. Hold them up while I count." The count is 10 seconds.

Do not let the person being tested drop his chest onto the table or rest his elbows. Watch for pronounced muscular development on one side of the spine. If this condition is present, the back should be checked from time to time to guard against scoliosis. Holding for 10 full seconds is passing, and is marked as "10." Anything less than 10 seconds is recorded as that part of 10 seconds that was held. For example, a person staying up for 4 seconds would get the mark of "4."

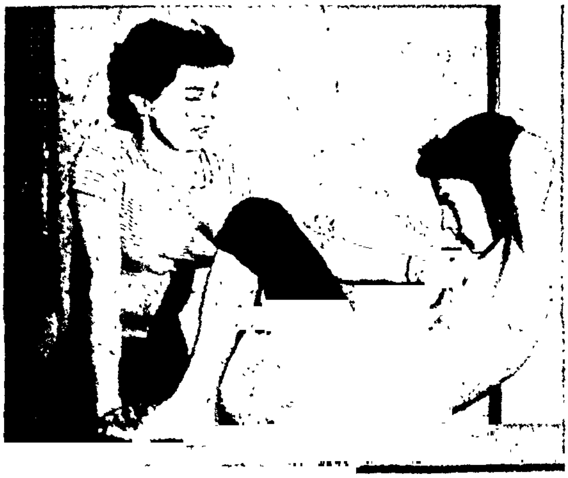

Fig. 4.–Test of strength of abdominal minus psoas muscles.

In the second test of the strength of the lower back (fig. 6), the person being tested remains prone over the pillow but removes his hands from behind his neck, places them down on the table, and rests his head on them. The instruction is as follows: "I am going to hold your chest down on the table. Try to lift your legs up but do not bend your knees." There may be a tendency to bend the knees or even to support the legs by keeping the toes on the table. It may be necessary to assist him in the required position. "Now, hold this position while I count 10." Marking is the same for the other tests. The last test is of the length of back and hamstring muscles (fig. 7). The person being tested is standing erect in stockinged or bare feet, hands at his sides. The instruction is as follows: "Put your feet together, keep your knees straight, now lean down slowly and see how close you can come to touching the floor with your finger tips. Stay down as far as you can for a count of three. Do not bounce."

Watch out for bouncing. The furthest point reached without bouncing and held for three counts is the marking point. The examiner should hold the knees of the person being tested in order to prevent any bend. Touch is designated with "T." "Touch" is only given when the floor-touch is held for three counts. Less than "Touch" is marked by the distance in inches between the floor and the finger tips. For example, a person unable to touch the floor by 2 in. would be marked "–2."

Test Results

When the Kraus-Weber tests were first given to American school children we thought that our minimum standards might be too high to be met by the average school child, but the European results indicated that this was not necessarily so. It seemed that our American standard of living was too high. We do not balance our modern mechanized conveniences with a reasonable amount of compensating physical activity. There are not many men left who have drawn water or hewed wood, and as adult physical work becomes less arduous the children's chores become less demanding. As time goes on and new and better laborsaving devices keep being added to the market our general population becomes less and less physically active.

It is somewhat contradictory, therefore, to note that while the fitness level of the general public is steadily falling our specialized teams of selected star athletes are becoming more physically outstanding year by year. We are loud in admiration of their prowess, which we watch and applaud comfortably from our soft armchairs. Increasingly few of us get, or take, if offered the opportunity, much personal physical exercise. As we become ever more urban, the numbers of our sedentary workers increase, while our senses are continuously assaulted by emotionally packed stimuli from radio, television, movies, and world-wide news coverage. Our tensions increase steadily, and our physical exertion, which might help relieve them, as steadily decreases.

Jack Wickstrom, professor and chairman of the division of orthopedic surgery, Tulane University School of Medicine, declared that one of the biggest faults of the school system generally is that physical education is merely supervised play. Schools no longer carry out posture exercises and gymnastics.[11]"

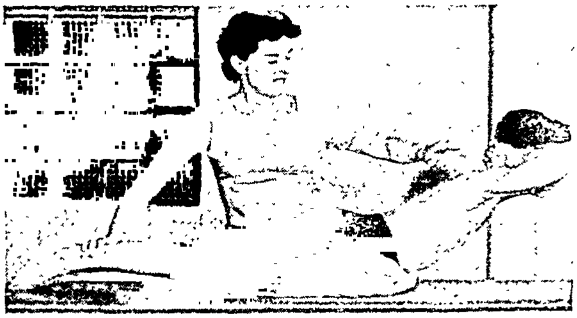

Fig. 5.–Test of strength of upper back muscles.

Three attitudes have been rather prevalent among pediatricians. One is that, as there may be a real danger in having a child with a physical impairment, particularly of the cardiorespiratory system, participate beyond his ability in strenuous competitive contact sports, they are against all fitness programs. You will all agree that the first part of any fitness program is a thorough physical examination by the pediatrician, who should advise the child and his parents as to any limitations in physical activity, and make certain that correctly designed protective equipment is properly worn. It is interesting to note that most of the problems arising from certain Little League programs are caused by adults participating too much in the program.

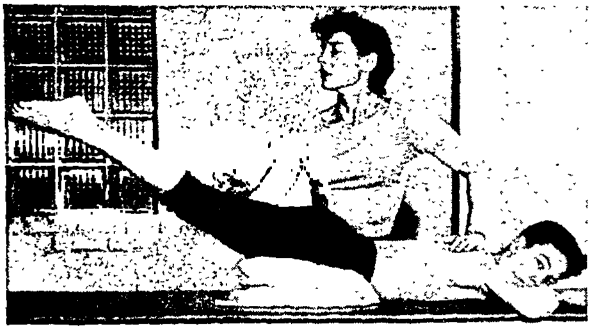

Fig. 6.—Test of strength of lower back.

Second, a few pediatricians have objected to the emphasis on physical fitness by claiming that it segments off a small part of total development, maintaining that there are other aspects of fitness, such as moral and educational. I heartily agree with this, but I feel that any competent pediatrician takes these matters into account in dealing with his patient and family. My chief concern is that the pediatrician play his rightful role in the fitness of youth. Lloyd Appleton, of the physical education department of the United States Military Academy at West Point,[12] has studied the relationship of physical fitness, as determined by the results of the physical aptitude entrance test, to future leadership and to discharge because of psychiatric disability. He found that those falling within the lowest 7% of the group on physical aptitude scores made up the largest number of those discharged for psychiatric reasons and that among those in the top 7% of the group there were no discharges for psychiatric disorders. The highest number of cadet leaders came from the upper 7%.

The third attitude among pediatricians is simply a disinterest in the fitness of youth as regards muscle strength and flexibility. I feel that this attitude can no longer be held, because of the tremendous publicity on and public interest in this problem. The week of June 1-7, 1958, was declared Youth Fitness Week by President Eisenhower. When the new president of the Junior Chamber of Commerce took office in Los Angeles, he stated that the J. C.'s were taking up the problem of the physical fitness of youth as the theme of one of their major programs this year. Anyone who is familiar with the dynamic leadership of this group knows that there will be great activity throughout the United States as a result of their interest in this problem.

Recommendations.—I have three recommendations. First, the pediatrician must take an active role in the physical fitness of American youth. There is a definite problem, with implications of a serious natural deficit, if the present laxity in physical education is allowed to continue. Various lay groups are becoming increasingly active in this field. The pediatrician must stand ready to give the needed advice, counsel, or leadership when necessary. He should emphasize the necessity of taking a complete history and physical examination prior to the child's participation in a fitness or sports program. Second, the pediatrician should encourage the use of the six Kraus-Weber tests as a basic screening device for detecting minimal physical competence. Third, the pediatrician should see that the schools in his area provide at least a minimal program of physical education, preferably of strenuous calisthenics.

Conclusions

The pediatrician should realize that he has responsibility for the mental and emotional care as well as the physical development of the child under his guidance. He impedes the healthy growth and development of the child if he considers physical fitness the special province of the educators and physical instructors. He can help parents inculcate in the child a healthy attitude toward physical activity, help youth groups develop programs of activity that build physical strength and fitness, and urge PTA groups to have organized physical training included in all school programs. Physical education programs should be incorporated into the curriculums of all schools, particularly those in crowded city areas where children are already deprived of sufficient physical activity. Finally, the pediatrician should help the child realize early in

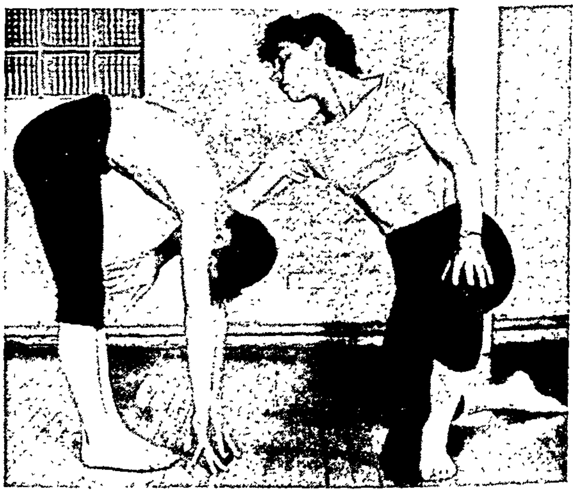

Fig. 7.—Test of length of back and hamstring muscles.

life that a flexible, strong body is vitally important for counteracting and combatting physical fatigue, emotional stress, and tension. He should help the child learn that a healthy, physically fit body requires, as do all the worthwhile things in life, hard work and sustained effort.

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REHABILITATION OF FARMERS WITH HEART DISEASE

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and
Warren L. Van Eschen, B.S., Cedar Rapids, Iowa

The occupational status of 43 men and 3 women with heart disease was studied with reference to the rehabilitative needs and potentialities of farmers. All were employed in agriculture, some with and others without changes or restrictions in their work. The most frequent diagnosis was arteriosclerotic heart disease. When reexamined one to two years later, the group showed no evidence of functional deterioration. A third examination, two to three years after the first, was possible in 30 members of the original group and gave the same result. Two patients had died of second attacks of myocardial infarction that had no apparent relation to the work they did. Methods of estimating functional cardiac capacity and prescribing a safe work load are still unsatisfactory, but this must not deter the physician from giving specific advice to agricultural workers with heart disease. He bases his recommendations not only on figures for energy expenditure and cardiac classification but also on his knowledge of the variables affecting the individual patient.

Increasing efforts are being made to meet the rehabilitation needs of cardiac patients employed in industry. The industrial work evaluation unit admirably serves this group of handicapped people, but similar concern has not been shown for those with cardiovascular disease who are engaged in agricultural occupations. The establishment of formal work evaluation units for rural people is not feasible in most areas for obvious reasons, but medical and social investigation and job analysis are no less urgent for those handicapped for agriculture than for those handicapped for industry.

This report describes the results of a team study of the utilization of community resources for aiding farmers with heart disease to solve their occupational problems. The primary purpose of the demonstration, carried out from 1955 to 1957, was to explore the feasibility of applying the principles and techniques of the industrial work evaluation unit in a rural setting, not for definitive study of a statistically significant group of patients.

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Read before the 31st Scientific Sessions, American Heart Association, San Francisco, Oct. 26, 1958.

Materials and Methods

Our demonstration was carried out in one typical rural Iowa county with a population of 19,550, 8,000 of whom lived on 2,000 farms. Eligibility for participation required employment in agriculture, an age of 16 years or more, a diagnosis of actual or suspected cardiovascular disease sufficiently stable to permit consideration for rehabilitation, and referral by the family physician. A thorough medical evaluation was done at the State University of Iowa Medical Center to establish a diagnosis and assign a functional and therapeutic classification. The county extension director served as the job analyst. A vocational counselor from the State Division of Vocational Rehabilitation substituted for the social worker in the usual work evaluation unit. They both visited all the patients on their farms one or more times.

The drudgery of farming has been greatly reduced through increasing mechanization, but it is estimated that 50% of general farm jobs still are done by hand labor. Even so, energy expenditure can be further reduced by work simplification and thoughtful emphasis on farm management. The specific technique of job analysis used by the county extension director is beyond the scope of this discussion, but his contributions were based on a detailed evaluation of each patient's farm buildings and land, equipment inventory, cropping and livestock practices, and work habits. He assessed the financial status, managerial ability, past performance, and future goals in each case. This type of information must be available before any specific suggestions can be considered for work simplification or managerial changes to reduce the physical stress of farm labor. The physician cannot secure this information; the modernly trained extension agent can. The vocational rehabilitation counselor is an ideal member of such a team, because he is accustomed to dealing with handicapped people and he brings with him the resources of his agency.

The energy costs of farm jobs in most instances exceed those of the majority of industrial jobs. We made use of the data of Passmore and Durnin[1] on the energy costs of selected farm jobs in arriving at suggested changes in work methods. We also used similar data made available to us during the progress of the extensive Farm Cardiac Project at Purdue University,[2] later summarized in a pamphlet by the American Heart Association.[3] It was necessary to consider the factors of weather and peak work loads as well, because they vary greatly with the seasons.

Our goal was to make realistic suggestions to enable physically fit patients to remain in an agricultural occupation if they so desired. If they did not, we offered help in the transition to some other work. Recommendations based on all findings were presented to the patient and his family at a conference attended by the family physician. Forty-six patients, three of them women, were studied between 1955 and 1957. The value and size of their farms were comparable to the averages for the county and state as a whole. Their educational background was below the average.

Results

The patients' ages ranged from 17 to 77 years. More than half were between 40 and 59 years old. Specifically, 1 was in the second decade, 1 in the third, 7 in the fourth, 14 in the fifth, 11 in the sixth, 8 in the seventh, and 4 in the eighth. The types of heart disease represented are as follows: congenital heart disease (atrial septal defect), 2; rheumatic heart disease, 9, with predominant lesion as mitral stenosis in 1, mitral insufficiency in 3, aortic stenosis in 1, and aortic insufficiency in 4; arteriosclerotic heart disease, 16, with angina pectoris in 4 and healed myocardial infarction in 12; undetermined etiology (manifested by cardiac enlargement and/or history of cardiac failure), 9; hypertensive heart disease, 2; heart disease due to thoracic deformity, 1; neurocirculatory asthenia, 2; and no heart disease, 5.

Functional and Therapeutic Classification of Farmers with Heart Disease *

	Results	
	Initial, No.	After 1-2 Yr., No.
No heart disease	5	5
1-A	6	6
1-B	4	4
2-B	9	9
2-C	14	18
2-D	1	0
3-C	1	1
3-D	5	3
4-E	1	0

* Classification of the American Heart Association.

The functional and therapeutic classification, shown in the table, indicates that two-thirds of the patients had significantly limiting disease when they came under study: 31 were given the classification of functional class 2 or below. It can be seen also that medical reevaluation one to two years later indicated that the functional status had not deteriorated. In fact, four patients, initially classified as being below class 2-C, had improved.

A follow-up study, directed by Dr. William E. Connor, was completed in August, 1958, in 32 of the 46 patients two to three years after they joined the group. Two men who had had myocardial infarction died from second attacks, but there was no apparent relationship with the limited work they did. There has been no evidence of aggravation of the cardiac disease in the remaining 30 patients.

The results from this method for dealing with the occupational problems of the group do not require detailed description. In summary, they are as follows for 46 subjects: (1) farm without specific changes, 11 (5 without heart disease and 6 in class 1-A); (2) farm by specific use of outlined work simplification measures and changes in farm management, 10 (4 in class 1-B and 6 in class 2); (3) farm by major changes in farm operation, 2 (both in class 3); (4) retain farm interests by entering into or formalizing existing partnership or lease arrangements to shift major work loads, 7 (5 in class 2, 1 in class 3, and 1 in class 4); (5) rehabilitation by surgery for mitral stenosis, 1 (in class 2); (6) farm temporarily by use of family or hired help to gain time for maximum social security benefits (social security participation for farmers began in 1955), 3 (1 in class 2 and 2 in class 3); (7) discontinue farming and seek more sedentary work, 5 (4 in class 2 and 1 in class 3); (8) retire because of age, disability, and financial status, 5 (all in class 2); and (9) restrict activity to housework and introduce work simplification measures in the home, 2 (both women, both in class 2).

We considered more than energy expenditure and functional cardiac classification in recommending these dispositions. These people possessed all the variables common to human beings generally. Compliance with the advice was excellent.

Comment

This team approach and these techniques are feasible in helping farmers with heart disease to solve their occupational problems. Patient, family, and physician cooperated excellently. The results indicate that the demonstration was medically safe and agriculturally sound. Details of the application of such a multidisciplinary approach will vary with local circumstances, but the results of this demonstration indicate that here, at least, is one practical way to deal with an unmet rehabilitative need. Physicians should not delay giving specific advice to agricultural workers with heart disease who find it necessary to limit their activity just because further refinement in the accuracy of estimating functional cardiac capacity and relating it to the energy expenditure of a safe work load is needed. The physician is the key to the problem. He must bring the patient, the extension agent, and the vocational counselor together. Our experience demonstrates that farmers ask the extension agent for help in solving many of their agricultural problems but the partially disabled are not accustomed to seek specific advice for planning a safe work program. Medical guidance of the kind we have demonstrated will help adjust the farmer to his work and improve his opportunity for health.

This study was supported by grants from the Iowa Heart Association and the American Heart Association.

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LATE SEQUELAE OF SADDLE BLOCK ANESTHESIA IN OBSTETRICS

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and
William K. Jordan, M.D., Little Rock, Ark.

Evidence of neurological damage attributable to saddle block anesthesia was sought in the records of 3,147 obstetric patients who received this type of anesthesia in 1946-1951. Careful long-term follow-up was possible in 1,077 patients. Only six of these had findings that might be related to the anesthesia. These findings were usually altered reflexes, sensory changes in the legs, headaches, and dizziness. No major sequelae were found. In this series of patients the slight disadvantages of saddle block anesthesia were far outweighed by its advantages, especially its effectiveness, safety, and acceptance by patients and physicians.

Prior to 1946, several authors[1] described a technique of spinal anesthesia for relief of pain in labor and delivery, with a hyperbaric solution of dibucaine (Nupercaine) hydrochloride which they called "saddle block anesthesia." Since that time, saddle block anesthesia has become increasingly popular in the field of obstetrics. This method offers advantages to the mother, infant, nursing staff, and physician. There must be some merit in any anesthesia which is as popular as saddle block anesthesia has apparently become, as more than 200,000 obstetric cases with saddle block anesthesia have been reported in the literature since 1946.

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Read before the Section on Obstetrics and Gynecology at the 107th Annual Meeting of the American Medical Association, San Francisco, June 26, 1958.

On the other hand, there have appeared in both the obstetric and neurological literature certain unfavorable reports on late neurological complications after saddle block anesthesia. Our enthusiasm for this type of anesthesia must then be tempered if acute or late neurological sequelae develop in significant numbers. The complications after saddle block anesthesia may be acute or immediate, such as hypotension, postanesthetic headache, meningismus, and aseptic meningitis, or late neurological complications represented by chronic headaches, paresthesias, and transient or permanent paralysis.

Review of Literature

In 29,484 cases reported in the literature, there were no major sequelae due to saddle block anesthesia. Seegar and Devlin[2] reported 5,250 cases in seven years at St. Agnes Hospital, Baltimore. Follow-up of the patients proved difficult, but none of the physicians reported serious sequelae or mortality resulting from the saddle block anesthesia. Hospital records showed no mortality or paralysis, transient or permanent. They concluded, "We believe that paralysis from saddle block anesthesia is rare, and that until better obstetric anesthesia is offered, it is far safer than inhalation and more satisfactory than local anesthesia."

Sadove and Levin[3] reported 10,000 patients delivered by saddle block anesthesia without permanent paralysis, but they do not mention the length of time of their follow-up. Reed,[4] reporting 174 cases of cesarean section done with the patient under spinal anesthesia says, "There have been no neurologic complications. Specifically, no case of arachnoiditis has developed in our cases." Makepeace[5] was able to follow 1,606 out of 1,840 patients by letter, asking them to come for examination. Only 375 responded. These represented 425 spinal anesthesias. Only one patient had any neurological symptoms, having had meningismus attributed by one consultant to drug sensitivity. Two other patients complained of less severe degrees of transitory meningismus. Makepeace feels that it is reasonable to presume that no damage due to the anesthetic was found in the entire group, as none existed in the group which returned for examination.

Stanley[6] reported 1,000 cases of saddle block anesthesia without any permanent paralysis. Conti and Natali[7] also reported 2,607 cases of saddle block anesthesia with no known neurological sequelae. Dripps and Vandam,[8] in 1954, reported 10,098 spinal anesthesias given on their surgical service. There were no instances of incapacitating neurological disease, although headaches had occurred in 15% of the females. The few immediate neurological complications in their series disappeared within a few weeks, the longest lasting six months.

On the other hand, several highly unfavorable reports have appeared in the literature implicating saddle block anesthesia in late major neurological sequelae (29 incidents in more than 22,000 cases). So critical have these been that serious doubt as to the safety of this agent has been raised.

Nicholson and Eversole[9] found five patients with major neurological sequelae in 21,000 cases of saddle block anesthesia given for general surgical procedures. Kennedy and co-workers[10] reported 12 patients with grave paralysis admitted to Bellevue Hospital after spinal anesthesia. They conclude that "Paralysis below the waist is too high a price for a patient to pay in order that the surgeon should have a fine, relaxed field of operation," and again that "This anesthesia should be reserved for those patients unable to accept a local or general anesthesia."

Bergner and associates[11] of the University of Tennessee reported six cases of paralysis after saddle block anesthesia occurring during 1949 and 1950. Rosenbaum and co-workers[12] at St. Louis University, in 1952, reported 6 cases of adhesive arachnoiditis in 1,772 patients who had been given heavy dibucaine saddle block anesthesia, also during 1949 and 1950. Paralysis had developed three months to four years after the anesthesia. They were able to follow up 358 of the 1,772 patients. They state in their conclusions that "Spinal anesthesia is too dangerous to justify its use in the un-complicated obstetrical cases."

Minnitt and Gillies[13] wrote "To say that one has not seen complications is only half an answer, because one has probably not looked for them." Babcock,[14] however, says that the dangers of saddle block anesthesia remain largely with the user, rather than the drug and the technique employed.

Results of Neurological Examination at Arkansas Hospital

Our interest in late sequelae of saddle block anesthesia was stimulated by these reports in the literature. We had not noted any serious acute complications, but it was felt that some of the late sequelae might have been missed because patients had not been followed up neurologically for long periods of time. Consequently, we undertook a survey of all patients who had received saddle block anesthesia five or more years ago (Jan. 1, 1946, through Dec. 31, 1951); consequently, some of the patients were examined 10 years after their first spinal anesthesia.

Saddle block anesthesia, primarily with use of hyperbaric solution of dibucaine hydrochloride as an intrathecal injection toward the end of labor, was employed 13,299 times in this hospital during this six-year period. Due to a lack of 24-hour coverage by trained anesthetists in the birth room, saddle block anesthesia for delivery has been given by students and interns, under the supervision of residents, since 1946. Techniques were worked out to avoid the hazards of acute complications.

The records of 3,147 patients were reviewed. It was found that 25 were dead of causes not related to saddle block anesthesia. Two-thirds, or 1,998, could not be located; 47 who were located were unable to return for examination. The department of neurology developed a preliminary neurological screening examination procedure, and this was given to the remaining 1,077 patients. They were questioned regarding dizziness on change of posture, unexplained headache, stumbling, and urinary incontinence. They were examined for muscle strength and coordination, by having them stand on the toes of both feet and then on each foot separately. They were also examined for paresthesias, abnormal reflexes, stretch reflexes (tendon), Babinski signs, changes in deep sensation, and relaxation of rectal sphincter.

Table 1.—*Evidence of Patient Acceptance of Saddle Block Anesthesia*

	Saddle Block Anesthesia	
Subsequent Use, No.	Patients Accepting in Subsequent Births	Total
1	309	309
2	235	470
3	146	438
4+	59	236
Single	328	328
Total	1,077	1,781

Of the 1,077 patients who returned for examination, 981 were found to be free of all evidence of neurological abnormalities, either by history and/or neurological screening examination. There were 96 patients in whom some suggestive evidence of neurological abnormality was found. These patients were referred for complete neurological examination by members of the department of neurology. Sixty patients were thought to have altered reflexes on preliminary screening examination, but this was confirmed in only three by the neurological examination. The neurologist considered that the headaches and dizziness in only one of the 56 patients who complained of these symptoms was related to the saddle block anesthesia. The paresthesias in 2 of the 11 patients with suggestive sensory changes were thought to be due to the saddle block anesthesia, while in the other 9 patients it was due to other causes. Some patients had one or more of these signs and symptoms. Eleven of these 96 patients referred to the neurologist were unable to complete their neurological examinations for personal reasons.

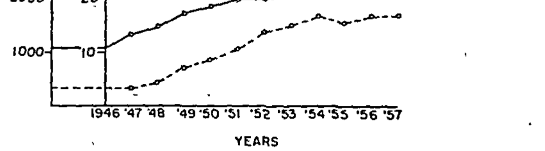
Only nine of the patients referred for neurological examination were found to show significant neurological deviations. An analysis showed that six of the nine had findings which were probably related to saddle block anesthesia. These consisted of absent or markedly decreased reflexes in three patients, sensory changes in the legs in two, and headaches and dizziness in one. In the other three patients, there was some question as to the relation of their symptomatology to saddle block anesthesia. Two of them had herniated disks, one in the thoracic region and one in the lumbar region. The third patient had severe headaches and dizziness for five years prior to, and continuing since, her first saddle block anesthesia. The neurologists were unable to find any neurological changes and felt that her headaches and dizziness were not caused by the anesthesia but may have been exaggerated by it.

Therefore, of the 1,077 patients examined, 9, or less than 1%, showed even suggestive changes on neurological examination which might be related to the saddle block anesthesia, and only 0.5% which were probably related to their anesthesia. This is an unusually low rate for late anesthetic complications of any kind. Our clinical experience does not indicate this method to be a hazardous form of anesthesia in obstetrics.

Comment

Though no case of serious complications resulted from saddle block anesthesia in our experience with 3,147 patients, the neurological screening examinations did reveal a rather large number of patients who had suggestive neurological complaints and signs of neurological changes. All but nine of these patients were cleared by the neurologist of deviations. In none of these patients had the symptoms been significant or incapacitating, and the 11 women who did not return for completion of the neurological examination refused because of their work schedule. The careful neurological examination identified only six patients with "probably related" and three patients with "possibly related" neurological deviations.

Since our study was made five or more years after the patients had received their first saddle block anesthesia, and as many of our patients are young women with recurrent pregnancies, many patients had had several saddle block anesthesias between the time of the termination of this study and the time of the examination. Some of the patients in the study group received as many as six subsequent saddle block anesthesias. The 1,077 patients examined in 1956 and 1957 had received 1,781 saddle block anesthesias at the time of the record review (table 1).



Incidence of saddle block anesthesia in obstetrics at University of Arkansas School of Medicine, 1946-1957.

An analysis of the frequency of employment of saddle block anesthesia reveals that its use is increasing at our hospital. Forty per cent of the over 9,000 patients delivered in the years of this study (1946-1951) received saddle block anesthesia (70% of more than 13,000 from 1952 to 1957). It is noted that 31.7% of the patients delivered in 1946 at our hospital received saddle block anesthesia, while 78% of the patients in 1954 were given it (table 2 and figure).

TABLE 2.—*Incidence of Saddle Block Anesthesia in Obstetrics, 1946-1951, 1952-1957*

		Saddle Block Anesthesia	
Yr.	*Total* Births	No.	%
1946	1,065	338	31.7
1947	1,314	339	25.8
1948	1,481	440	29.6
1949	1,719	746	43.4
1950	1,840	893	48.5
1951	1,967	1,075	54 7
Sub totals	9,386	3,831	40 8
1952	1,964	1,384	69.5
1953	2,003	1,486	74.2
1954	2,169	1,689	77.9
1955	2,165	1,589	73.4
1956	2,459	1,646	68.2
1957	2,707	1,674	61.4
Sub totals	13,467	9,468	70.2

The greatly expanding use of intrathecal anesthesia for both obstetric and surgical procedures has established a large body of patients in whom unrelated neurological deviations might occur at a subsequent date. Makepeace,[5] in surveying the two series of late sequelae after saddle block anesthesia in 1949 and 1950 in St. Louis and Memphis, suggests that epidemic Coxsackie virus encephalitis might be responsible because of the geographical factor of the Mississippi Valley. In the interval after our study (1951-1957) several bizarre neurological manifestations have been noted at the University of Arkansas Medical Center, and these will be the subject of a subsequent report.

Conclusions

The records of 3,147 patients receiving saddle block anesthesia in 1946-1951 were analyzed, together with a careful long-term neurological follow-up of 1,077 patients. Six of the 1,077 patients exhibited neurological deviations which were probably related to saddle block anesthesia. These were minor, including alterations in reflexes, mild sensory changes in lower legs, headaches, and dizziness. No major neurological sequelae were found. Our experience would indicate that paralysis or severe complications from saddle block anesthesia are rare. This method of anesthesia given for delivery has proved to be clinically effective, safe, with a high degree of patient and physician acceptance. We believe that until better anesthesia is available, or until there is 24-hour coverage in the birth room by trained anesthetists, saddle block anesthesia is safer than inhalation anesthesia and more satisfactory for both patient and doctor than local anesthesia.

4301 W. Markham (Dr. Dodge).

The dibucaine used in this study was supplied as Nupercaine by Ciba Pharmaceutical Products, Inc., Summit, N. J.

Screening examinations were conducted by house officers of the Department of Obstetrics and Gynecology.

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CURRENT CONCEPTS OF THE MEDICAL MANAGEMENT OF ULCERATIVE COLITIS

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Ulcerative colitis, though presenting a difficult therapeutic problem, is capable of responding to prolonged and comprehensive medical management. The important therapeutic measures include rest, the use of sedatives and antispasmodics, nutritional and electrolyte repletion, transfusions of blood or plasma, injection of iron for iron-deficiency anemia, antibacterial medication, especially use of sulfonamides and skillful attention to the emotional problems. ACTH and various adrenal steroids are useful adjuncts to therapy, initiating and potentiating recovery, facilitating control of severe recurrences, and providing an opportunity for "total treatment." These compounds can be administered effectively for long periods with a relatively low incidence of serious complications.

While the cure of disease depends on knowledge of etiology and pathogenesis, numerous illnesses, including ulcerative colitis, may be managed effectively though their causes remain obscure. Ulcerative colitis continues to present a most formidable therapeutic problem. Nevertheless, advances in the management of nutritional and biochemical disturbances and in the treatment of infections, the use of corticotropin and the adrenal steroids, awareness of the contributory role of emotional disorders in the disease, and increased knowledge of the natural history of ulcerative colitis have improved the outlook significantly. The purpose of this paper is to review current concepts of the medical management of ulcerative colitis and to reemphasize their effectiveness.

The Nature of the Problem

Ulcerative colitis is an acute and chronic inflammatory and ulcerative disease of the colon and rectum.[1] The principal symptoms are rectal bleeding, diarrhea, abdominal discomfort, and cramping pain, fever, anorexia, and malnutrition. Proctoscopy usually demonstrates diffuse inflammation, congestion and edema of the mucosa, multiple tiny ulcerations, excessive bleeding, and bloody or purulent exudate. X-ray examinations reveal that the entire colon is affected in at least 50% of cases; varying segments of the intestine are diseased in 40%; and in 10% the process is relatively superficial and does not produce roentgenologically demonstrable changes. The adjacent terminal ileum is involved in perhaps 15 to 20% of patients. Ileocolitis affects chiefly the distal ileum, the cecum, and the ascending colon. Ulcerative colitis usually occurs among young people; most patients are below the age of 40 or 50 years, though no age is exempt. There is no sex predominance. A family history of ulcerative colitis is elicited in 5 to 10% of patients. Allergic disorders, such as hay fever, asthma, and drug sensitivity, are present in 20 to 30% of patients.[2] Other interesting associations are rheumatic fever, rheumatoid arthritis, and erythema nodosum.

The onset of the disease may be mild, with occasional rectal bleeding, or it may be severe, developing as an acute, febrile, toxic illness.[3] Fulminating ulcerative colitis is characterized by necrotizing inflammation of the intestine. The onset is abrupt, with high fever, toxemia, intense diarrhea, electrolyte depletion, dehydration, poor nutrition, and abdominal distention. In children the disease may begin very gradually; fever and anemia may be the principal symptoms and diarrhea may not be prominent initially. The circumstances at the onset of ulcerative colitis usually are obscure. The disease often occurs in previously healthy individuals, frequently it develops in chronological association with acute enteric or respiratory infections, pregnancy, or serious emotional difficulties.

Chronic ulcerative colitis is a disease with striking tendency to recurrence. Remissions are common in mild and moderate colitis but are relatively infrequent in the untreated severe disease. Recurrences are related to upper respiratory and viral infections, other intercurrent illness, operations, the use of antibiotics as in the treatment of respiratory infections, the menses, pregnancy, dietary indiscretions, physical fatigue, and emotional tension. Complications develop in the majority of patients, significantly influencing the course of the illness and the response to treatment. In the colon, the problems include giant ulceration, perforation, peritonitis, pericolitis, "toxic megacolon," hemorrhage, stricture, obstruction, pseudopolyps, polyps, carcinoma, perirectal abscess, fistula, electrolyte depletion, and defective absorption of food. The systemic complications include anemia, nutritional deficiencies, hypoproteinemia, hypergammaglobulinemia, rheumatoid arthritis, thrombophlebitis, uveitis and iritis, erythema nodosum, pyoderma gangrenosum,

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pyelonephritis, nephrolithiasis, fatty liver, hepatitis, cirrhosis of the liver, pancreatitis, adrenal depletion, osteoporosis, acute psychosis, hemolytic anemia, drug sensitivity, transfusion reactions, and amyloidosis. The number of complications in a single case may be considerable, as in a male patient who developed biliary cirrhosis, ascites, pancarditis, erythema nodosum, anemia, hypoproteinemia, steatorrhea, osteoporosis, acute arthritis, pyoderma, rectal fistula, and polyps. The mortality varies from 5 to 20% depending on the severity of the cases analyzed. Fatalities are more frequent during the first one or two years of illness, especially in patients with fulminating colitis. The more important causes of death are perforation of the intestine with peritonitis, hemorrhage, overwhelming infection, carcinoma of the colon, and surgical complications.

Despite considerable investigation, the cause of ulcerative colitis remains unknown.[4] Many causes have been postulated, including allergy to foods, nutritional and hormonal deficiencies, lymphatic obstruction, absence of "protective factors" in the intestinal wall, bacterial or viral infection, the destructive action of proteolytic enzymes or bacterial endotoxins, immunologic disorders including the Shwartzman and Arthus phenomena, antigen-antibody reactions and autosensitization of the colon, vasospastic, neurogenic, and psychogenic disturbances, abnormalities in the connective tissue of the intestinal wall, and metabolic disturbances. The irritable colon does not predispose to ulcerative colitis. Though amebic dysentery may rarely be followed by ulcerative colitis, parasitic infestations and bacillary dysentery do not predispose to the disease. Multiple causal factors probably are involved; on the basis of our clinical and laboratory observations an immunologic component, perhaps autosensitization of the colon, with or without the action of bacterial endotoxins, is a possibility; neurogenic stimulation of the intestine with vasospasm and secondary infection also appear important.

Objectives of Therapy.—The treatment of ulcerative colitis remains nonspecific, symptomatic, and comprehensive. Since the anatomic changes often are severe, and healing requires long periods of time, treatment must be prolonged. Certain therapeutic principles apply generally, but variations in the course of the disease necessitate adaptation of the program to the individual patient. The immediate objectives are physical and emotional rest, maintenance of nutrition, elimination of infection, restoration of normal intestinal function, and control of the associated emotional problems.[5] The ultimate goal, of course, is complete healing of the intestine and return of the patient to a normal life. The potentiality for reversibility in ulcerative colitis is considerable, perhaps greater than is appreciated, and this possibility provides the basis and the justification for continued medical management. The protracted illness, the many complications, and the frequent, expensive hospitalizations are understandably discouraging to the patient and his family. A lucid explanation of the illness and its treatment and a hopeful prognosis are helpful in securing the cooperation necessary for the prolonged therapy. Patience, perseverance, and equanimity are required of the physician undertaking the management of this difficult problem.

Rest, Sedative, and Antispasmodic Therapy

Physical fatigue and emotional tension contribute to the persistence and recurrence of ulcerative colitis. Rest and adequate relaxation diminish spasm and hyperactivity of the colon. Complete rest in bed in the hospital is indicated during the acute stage; hospitalization permits careful control of the patient and the environment and the establishment of an effective therapeutic program. In some cases hospitalization of three to six months or longer may be necessary to control the disease thoroughly. Adequate rest may be obtained through a combination of skillful nursing, long hours of sleep, and pleasant recreation. Sedatives, especially barbiturates such as phenobarbital (30 mg. four times daily), are helpful. Various tranquilizing drugs and appropriate dosages include hydroxyzine (Atarax) hydrochloride, 25-100 mg. four times daily; prochlorperazine (Compazine), 5-20 mg.; thiopropazate dihydrochloride (Dartal), 5-30 mg.; meprobamate (Equanil or Miltown), 4-800 mg.; promazine (Sparine) hydrochloride, 10-200 mg.; chlorpromazine (Thorazine) hydrochloride, 10-200 mg.; perphenazine (Trilafon), 2-16 mg.; and phenaglycodol (Ultran), 3-600 mg. Chloral hydrate, 1 Gm., secobarbital (Seconal), 100 mg., pentobarbital (Nembutal), 100 mg., Tuinal, a combination of equal proportions of sodium seconal and sodium amytal, 100 mg., and glutethimide (Doriden), 0.5 Gm., are among many compounds which can be prescribed at bedtime to facilitate sleep.

Antispasmodics tend to reduce spasm and hypermotility of the intestine, though their effects are extremely variable. Tincture of belladonna, 10 drops four times daily, and atropine sulfate taken orally, 0.005 Gm. several times daily, have long been prescribed for this purpose. Many other effective antispasmodic, anticholinergic drugs are available; including diphemanil (Prantal) methylsulfate, 100 to 200 mg. four times daily; piperphenamine (Darstine), 100 mg.; penthienate bromide (Mondronal), 5 mg.; propantheline (Pro-banthine) bromide, 15 to 30 mg.; oxyphenonium bromide (Antrenyl), 10 mg.; methscopolamine (Pamine), 2.5 mg.; tridehexethylchloride (Pathilon) chloride, 50 to 100 mg.; and hexocyclium methyl sulfate (Tral), 25 mg.

To suppress the hyperactive gastrocolic reflex, these drugs are prescribed more effectively before meals and at bedtime. The individual response and the clinical tolerance for anticholinergic compounds varies considerably, necessitating selection of the drug most useful in each case. In severely ill, malnourished patients and in children, the potent antispasmodics may suppress intestinal motility so completely as to produce atony. The abdominal distention and absence of audible peristaltic activity, together with the fever, may suggest peritonitis; however, intestinal motility usually returns within 48 to 72 hours after the medication is discontinued.

Severe abdominal cramping pain and rectal tenesmus temporarily may require the use of deodorized opium tincture (10 drops three or four times daily), codeine sulfate (0.03 Gm. four times daily), morphine sulfate (0.015 Gm.), or meperidine (50 to 100 mg.). Opiates are not prescribed routinely or for long periods, to avoid the possibility of addiction; opiates, by increasing intestinal spasm, occasionally intensify rather than lessen the abdominal discomfort. Heat applied to the abdomen by means of an electric pad or hot water bottle also relieves the abdominal discomfort. The prolonged diarrhea of ulcerative colitis may cause anal irritation; compresses of witch hazel, hot sitz baths, and local anesthetic ointments will relieve the discomfort and facilitate healing.

Management of Emotional Problems

Ulcerative colitis does not appear to be primarily of psychogenic origin, but emotional disturbances are demonstrable in the majority of cases, if not in all. The patients are described psychiatrically as dependent, immature, self-depreciating, obsessive-compulsive, hostile individuals, highly vulnerable to the ordinary events of life, perhaps because of feelings of humiliation, loneliness, helplessness, and hopelessness.[6] The psychiatric problems occasionally involve severe depression, schizophrenic and paranoid reactions, and suicidal attempts. The specificity of the emotional difficulties and their importance in the pathogenesis of ulcerative colitis require further elucidation. The psychogenic factors may reflect an important predisposition to the disease, or they may represent the secondary emotional manifestations of prolonged physical illness, disappearing when the disease is controlled or cured. Nevertheless, the emotional difficulties influence the course of the disease and the therapeutic response adversely. Thorough knowledge of the patient's emotional problems and skillful management of them are indispensable to the effective treatment of ulcerative colitis. On the other hand, the resultant symptomatic improvement does not necessarily establish the causal importance of the psychogenic factors.

Formal psychotherapy is indicated for the seriously disturbed patient. Though its permanent value has not been established conclusively, the approach often is helpful, especially in cooperation with the internist. Caution is necessary during the acute stage of ulcerative colitis, for the patient then is unable physically and emotionally to deal effectively with his problems; the resulting conflicts may aggravate the colitis and precipitate serious complications. Emphasis exclusively on the psychiatric aspects is unwise because of the hazard of inadequately treated or unrecognized organic disease; a case in point is that of a young man who previously had undergone operations for regional enteritis and intestinal obstruction. Persistent severe pain in the rectum had been attributed to an emotional disturbance and psychotherapy had been maintained for several months, though the patient had not been examined. Rectal examination easily demonstrated a large ulceration of the rectum with severe inflammation and muscle spasm; the pain subsided when the ulcer healed. Neglect of the psychiatric difficulties also is likely to retard the response of the patient. In general, the most helpful psychotherapy is administered by the well-informed, interested, and sympathetic attending physician, constantly providing reassurance and encouragement. The patient-physician discussions may disclose a difficult or frustrating problem at work or at home, readily dealt with on a common-sense basis, resolution of which may improve the course of the disease decisively. The objective of this approach is protective, ego-strengthening reorientation rather than fundamental reorganization of the patient's personality. Sustained physical and psychogenic improvement is reflected in the development of confidence, poise, and a more mature approach to life. Frequently, and especially in children, psychotherapy also must be directed to the parents. Indeed, the success of therapy may be determined by the ability to influence the family environment to the benefit of the patient. Psychoanalysis, in a small group of patients, apparently has not produced significant permanent benefit. The value of electric shock therapy[7] and lobotomy in patients with ulcerative colitis remains to be established.

Diet, Nutritional Considerations, Electrolytes, and Fluids

Ulcerative colitis is not caused by nutritional deficiencies, food allergy, or roughage in food. However, a diet without the mechanical and chemical irritants contained in fruits, vegetables, fruit juices, condiments, alcoholic beverages, and excessively hot or cold foods decreases the abdominal distress and the diarrhea. A more limited menu, consisting of farina, cream of wheat, toast, butter, soft boiled eggs, clear broth, tea, boiled rice, jello, and custard may be utilized temporarily in the acutely ill patient. A bland diet with meat and potatoes but without fruits and vegetables usually is prescribed initially. Cooked or canned fruits and vegetables are added when the feces are consistently well formed and do not contain occult blood. The diet is liberalized as the improvement continues. For psychological reasons dietary restrictions are less rigid for children with ulcerative colitis; indeed, the bland diet should not be permitted to assume overwhelming significance for any patient, as conflicts between the limitation of food and the psychogenic disturbances resulting therefrom should be resolved in favor of the emotional considerations. The clinical improvements associated with the avoidance of fruits, bran cereals, and milk seem attributable most likely to the elimination of high-residue foods; milk especially may increase the flatulence, abdominal discomfort, and diarrhea.

Nutritional deficiencies are very common in ulcerative colitis, as a result of the reduced intake of food, the increased tissue catabolism, loss of blood, and the tremendous loss of nitrogen in the feces. The importance of restoring normal nutrition in patients with ulcerative colitis hardly can be overemphasized; in some cases this alone may suffice to initiate significant improvement. The diet, therefore, should provide adequate amounts of proteins and calories, perhaps 2,500 to 3,500 calories including 125 to 150 Gm. of protein daily. Supplements may be added, though good-quality whole foods are preferred. Protein anabolic agents, such as testosterone propionate and norethandrolone (Nilevar), may be prescribed to increase the retention of nitrogen in the tissue. The cooperation of a competent and interested dietitian is invaluable in providing appetizing menus and in encouraging the patient to eat sufficient quantities of food. Complete nutritional restoration requires at least three months and often longer. Rapid transit of food through the hyperactive intestinal tract and concomitant disease of the ileum may interfere with normal absorption, resulting in steatorrhea. The presence or absence of malabsorption is indicated by measurements of the plasma carotene and fat excretion in the feces. In the presence of steatorrhea, the fat intake may be limited to 75 or 50 Gm. daily; adrenal steroids are useful in the management of this problem. Tube feeding with protein supplements or liquefied homogenized foods, and concomitant constant suction of the distal small intestine, may be helpful in selected cases, but this procedure rarely has been necessary in my experience.

The severe diarrhea of ulcerative colitis causes excessive losses of potassium, sodium, and chloride from the intestinal contents and dehydration. Solutions of 5% dextrose in isotonic sodium chloride solution, containing appropriate quantities of potassium salts, are necessary to correct the electrolyte and fluid deficiencies. Fluids may be administered for long periods via a polyethylene catheter introduced into a small vein; however, this procedure is potentially hazardous because of the possibility of secondary infection, especially in patients receiving steroids, and it is not recommended in patients receiving both antibiotics and steroids. Measurements of the fluid intake, urine output, and of the serum electrolytes provide useful information. Complete reliance on these indexes probably is unwise, for the serum sodium and potassium may be normal, at least temporarily, in the presence of depletion of electrolytes. The excessive loss of calcium in occasional patients with steatorrhea necessitates the intravenous administration of calcium salts.

Transfusions of whole blood, 500 to 1,000 ml., are indicated for moderate or severe hemorrhage and for anemia and hypoproteinemia; the amounts required may be estimated from the hemoglobin, erythrocyte count, hematocrit, and, if available, the blood volume. The frequency of transfusion reactions in the colitis patient necessitates the most careful blood typing and cross matching; the blood should preferably be administered slowly at room temperature. Addition of an antihistaminic may reduce the incidence of reactions. Plasma, 500 to 1,000 ml., stored at room temperature, and human albumin, 50 Gm. injected intravenously, are useful in correcting hypoproteinemia when the food intake is low. Protein hydrolysates probably are less satisfactory for this purpose because of rapid metabolism, but they may be administered. The newer intravenously given fat emulsions provide an additional source of food and calories; substantial amounts may be administered without apparent untoward effects. Iron-deficiency anemia is very common as a result of the reduced intake of food and the chronic loss of blood from the intestine. In the absence of profuse rectal bleeding, anemia may be corrected by intramuscular administration of an iron-dextran complex (Imferon), 1.0 to 2.0 Gm., in divided doses; the hematological response is evident within several weeks. Iron administered orally is often irritating to the gastrointestinal tract in patients with ulcerative colitis, though several newer preparations are alleged to be less troublesome in this respect and ferrous sulfate taken orally with meals may be tolerated by some patients. Multivitamins are useful nutritional adjuncts; B complex preparations may be added to the intravenously given fluids or injected intramuscularly. Excessive quantities of vitamins are unnecessary; preparations such as ascorbic acid are irritating to the intestine when taken by mouth. Severe bleeding in ulcerative colitis usually originates in the highly vascular intestinal wall. Occasionally in patients with associated hepatic disease or with defective intestinal absorption the prothrombin time may be prolonged, contributing to the bleeding, but the parenteral administration of vitamin K will correct the abnormality.

Sulfonamides and Antibiotics

Although a bacterial or viral causative factor has not been established, the fever, the inflammation demonstrable proctoscopically and histologically, and the toxemia and complications such as perirectal abscess and pericolitis suggest an intestinal infection. There is no consistent correlation between the identifiable bacterial flora of the intestine and the clinical course of ulcerative colitis, although occasionally the subsidence of symptoms coincides with the disappearance of hemolytic coliforms, staphylococci, and streptococci from the feces. Sulfonamides may be prescribed in ulcerative colitis to control or prevent secondary infection and in the hope of eliminating unidentified bacterial causes of the disease. Sulfonamides may also be administered during the use of ACTH and the adrenal steroids to prevent secondary infection. The total bacterial count in the feces will decrease as a result of eliminating the coliform organisms, and the fecal flora will change from gram-positive to predominantly gram-negative. The long-term effects of prolonged sulfonamide therapy on the bacterial flora of the feces have not been studied thoroughly.

No single sulfonamide excels all others, in my experience, although several appear to be especially useful. These include sulfaguanidine, 8 Gm. daily; salicylazosulfapyridine (Azulfidine), 4 to 8 Gm.; phthalylsulfathiazole (Sulfathalidine), 4 to 6 Gm.; succinylsulfathiazole (Sulfasuxidine), 8 to 12 Gm. daily; sulfadiazine and sulfisoxazole (Gantrisin) 4 to 6 Gm. daily. The sulfonamides usually should be administered continuously rather than intermittently. Soluble compounds, such as sulfadiazine, may be given as retention enemas in doses of 1 or 2 Gm. in 30 or 60 ml. of water or isotonic sodium chloride solution; beneficial results are noted in patients with relatively localized colitis. Para-nitrosulfathiazole (Nisulfazole) may be administered rectally as a 10% suspension in quantities of 1 or 2 oz. (28 or 57 Gm.). The beneficial clinical effects during sulfonamide therapy are observed initially in numerous cases and may continue for weeks, months, or years. More often, however, the response gradually decreases, presumably because either the original flora are restored or resistant bacteria develop. A change in sulfonamide may renew the clinical response; sulfonamide drugs thus may be alternated effectively for long periods. Sulfonamides may cause adverse side-effects, including fever, nausea, vomiting, flatulence, and headache, and dermatological, hematological, and renal complications, although their incidence is relatively low. The temporary antibacterial effects, the development of bacterial resistance, and the variable clinical responses are important limitations. Nevertheless, the sulfonamides seem to be helpful adjuncts, probably contributing to the control of the disease and decreasing, though not eliminating, the hazard of serious infection.

Penicillin (1 to 2 million units daily) and streptomycin (1 to 2 Gm. daily) may be administered intramuscularly together for the same reason as the sulfonamides. They seem indicated during the acute febrile stage of the illness and in the management of pericolitis when medication by mouth is discontinued temporarily. The antibacterial effects of chlortetracycline (Aureomycin), chloramphenicol (Chloromycetin), oxytetracycline (Terramycin), tetracycline (Achromycin), and neomycin sulfate resemble those of the sulfonamide drugs: tetracycline and neomycin sulfate perhaps are the most effective of this group. The clinical response occasionally may be favorable, but since these compounds cause disturbing gastrointestinal side-effects, including glossitis, stomatitis, nausea, flatulence, diarrhea, perianal itching, and a proctitis, not unlike ulcerative colitis, they are not prescribed routinely. An exception to this principle is the very occasional use of tetracycline (1 Gm. by mouth daily) for pyoderma. The use of antibiotics, including penicillin administered orally, in the treatment of respiratory infections among colitis patients should be avoided because of the possibility of aggravating or reactivating the disease.

Corticotropin (ACTH) and Adrenal Steroid Therapy

The use of corticotropin (ACTH) and the adrenal steroids in ulcerative colitis is based on several considerations, among them the limitations of conventional treatment, the chronicity and progression of severe colitis, and the numerous complications, including rheumatoid arthritis, erythema nodosum, myocarditis, and iritis, responsive to corticoid therapy. ACTH and the adrenal steroids do not cure ulcerative colitis, prevent recurrences completely, or replace established methods of treatment, but they are useful, at times dramatic, adjuncts when administered in sufficient quantities for adequate periods of time and under carefully supervised conditions.[2] The improvement produced is similar to that observed in the absence of steroids but it is more frequent, more rapid, and more complete. The response is characterized by the prompt disappearance of fever, toxemia, abdominal discomfort, and diarrhea; by increased appetite and by a remarkable sensation of well-being. While the psychological benefits are not inconsequential, the steroid effect involves demonstrable healing, as noted in histological studies of rectal biopsies. The proctoscopic changes subside gradually; the rectal mucosa eventually may appear normal or slightly granular and hyperemic. Laboratory indications of the favorable response include the lowering of elevated sedimentation rates and the return of serum mucoprotein levels to normal, disappearance of blood from the feces, subsidence of the nitrogen loss in the feces, and restoration of the normal pattern of plasma proteins. Rectal biopsies demonstrate histologically the disappearance of edema, cellular infiltration, and ulceration, reconstitution of the normal ground substance of the connective tissue of the intestine, and restoration of the basement membranes of the epithelium of the colon.

The quantities of ACTH and the adrenal steroids required in ulcerative colitis exceed the amounts effective in other diseases; relatively large quantities for long periods are necessary to control the disease completely. Aqueous corticotropin, the most potent compound, should be administered intramuscularly in doses of 30 mg. every six hours, 120 mg. per day; 160 or 200 mg. daily may be given temporarily in selected cases. ACTH administered intravenously, in quantities of 10 or 20 U. S. P. units contained in 500 cc. of 5% solution of dextrose in distilled water, every 12 hours, is the most potent stimulant of adrenocortical function. Corticotropin gel or corticotropin-zinc hydroxide has been prescribed chiefly as maintenance therapy in single daily doses of 40 or 80 mg. The orally administered steroids in decreasing order of effectiveness in ulcerative colitis are hydrocortisone (200 mg. per day initially), prednisone or prednisolone (60 to 80 mg.), and cortisone (300 mg.). Hydrocortisone also may be given intravenously in quantities of 50 mg. every 12 hours, and intramuscularly in doses of 50 to 100 mg. every 4 or 6 hours. Steroids administered as retention enemas once or twice daily or by continuous drip appear to be helpful in some patients; the advantages of this procedure presumably are maximal concentration of the steroid in the diseased area and a lesser tendency to side-effects,[8] however, systemic steroid effects may occur when sufficiently large amounts of steroids are administered intrarectally. The preparations administered by this route include hydrocortisone sodium succinate (100 or 200 mg. in 15 to 250 ml. of water or isotonic sodium chloride solution) and prednisone (15 to 30 mg.) together with phthalylsulfacetamide and the newer steroid, methylprednisolone (Medrol, 60 to 80 mg. in 15 to 30 ml. of water). Clinical and proctoscopic improvements have been observed within 7 or 10 days. Opiates, including tincture of deodorized opium, codeine, or morphine, may be required to facilitate retention of the steroid solution. Hydrocortisone also has been prepared in the form of rectal suppositories, each containing 10 to 15 mg. and prescribed three or four times daily; the value of this type of medication is not yet established. Several new oral compounds, triamcinolone (Aristocort, Kenacort, 20 to 30 mg. daily) and methylprednisolone (20 to 32 mg. daily) are helpful occasionally. On the basis of present evidence, the effects of the new steroids do not appear to excel those of hydrocortisone or prednisone in ulcerative colitis. As with other medication, the response varies considerably among individuals and in the same patient at different times, necessitating identification of the steroid and the maintenance dose most effective for a given individual, as in the patient not responding to large doses of prednisone, or hydrocortisone, in whom symptoms subsided when given methylprednisolone.

The steroids are continued usually for several months and in many instances for years, as a practical means of maintaining patients in satisfactory health without surgery. The initial doses are decreased gradually, depending on the individual course. When the daily intake of ACTH reaches 40 to 60 units this compound may be replaced by hydrocortisone, prednisone, or one of the newer hormones. The transition is accomplished by arbitrarily exchanging 1 mg. of prednisone or 2 mg. of hydrocortisone for 1 unit of ACTH. Effective minimal or maintenance doses then are determined for each patient; these usually are for ACTH, 20 to 40 units daily; for hydrocortisone, 40 to 80 mg.; for prednisone, 15 to 30 mg.; for methylprednisolone, 12 to 20 mg.; and for triamcinolone, 12 to 20 mg. Periodic adrenocortical stimulation with corticotropin, though theoretically rational, has not appeared necessary. Recurrences during steroid therapy usually are related to respiratory infections, fatigue, tension, and especially to premature reductions in dosage. Occasionally, the therapeutic effect diminishes after the prolonged or intermittent administration of steroids. The mechanism of the waning response is not known; it may be related to increasing severity of the disease, the development of circulating antihormones, or partial inactivation of ACTH by tissue enzymes at the site of injection. However, a similar clinical tolerance may develop with the orally administered compounds. The response may be restored by increasing the quantity of medicament, by changing the compound, or by the readministration of corticotropin. In a patient 59 years of age the response to ACTH was excellent initially but nil during a subsequent recurrence; a similar trend was observed later with prednisone and with hydrocortisone. Currently, symptoms seem to be responding to triamcinolone but the outlook is uncertain, perhaps because of unresolved serious emotional problems. In 10 to 15% of patients with ulcerative colitis, steroids fail to influence the disease even temporarily; the factors involved are not known, though emotional disturbances seem to be important. In a small number of patients drug sensitivity or allergy to ACTH limits the use of this preparation.

ACTH and the adrenal steroids should not be prescribed routinely in ulcerative colitis, for numerous patients respond satisfactorily to symptomatic supportive therapy without the adrenal hormones. The principal indications are severe disease, recurrent despite thorough medical management in the hospital; acute fulminating colitis; and the presence of arthritis, iritis, and erythema nodosum. Steroids are contraindicated in the presence of perforation of the intestine, peritonitis, and abscess formation. In severe ulcerative colitis complicated by malnutrition, electrolyte imbalance, and overdistention of the colon, steroids should be prescribed with the utmost caution during the rapid correction of these conditions. Steroids are not contraindicated necessarily in the presence of hemorrhage or pericolitis with peritoneal irritation, for these complications may respond dramatically. Pseudopolypoid formation is not a contraindication, for a sustained favorable response to steroids may decrease the tissue hyperplasia significantly. A history of diabetes mellitus or tuberculosis does not exclude the use of hormones, provided the indications otherwise are acceptable and appropriate supportive therapy is prescribed. Peptic ulcer is not an absolute contraindication, for the incidence of ulcer during the steroid treatment of ulcerative colitis is low and colitis patients with a history of ulcer may take the hormones without apparent harmful effects.

Steroid therapy, in most cases, must be maintained for long periods, as premature reduction in dosage or discontinuation of medication is not infrequently followed by the relapse or recurrence of symptoms. Ideally, the steroids are discontinued when the feces contain no occult blood, bowel function is normal, the blood cell counts and sedimentation rates have returned to normal, and there is proctoscopic indication of healing. Roentgenologic evidence of healing, except for the disappearance of marginal serration and ulceration, is not to be expected in ulcerative colitis until after prolonged improvement. While the withdrawal of steroids may occasionally be difficult, the gradual discontinuation of medication in patients who have responded adequately usually is accomplished uneventfully.

ACTH and the adrenal steroids are capable of causing many complications.[11] The most common are the symptoms of adrenal cortical hyperfunction, or Cushing's syndrome (edema, moon-face, acne, "buffalo obesity," and hypokalemic hypochloremic alkalosis). Hypertension, hyperglycemia, glycosuria, and various infections, not uncommon with ACTH and cortisone, are less frequent with the newer compounds. Restriction of sodium chloride has been less necessary with the newer steroids. Emotional disturbances, including psychotic reactions, occur in 15% of cases and constitute an important but reversible complication. The development of steroid psychosis necessitates prompt discontinuation of the medication and sedation; chlorpromazine, 100 or 200 mg. daily, is especially valuable for this purpose. The striking improvement in the colitis during the psychosis is of interest.

Giant ulceration, perforation of the intestine, and hemorrhage, important complications of the disease in the absence of steroids, have not increased in frequency during hormonal therapy, in my experience. Persistent hemorrhage in ulcerative colitis usually is ascribable to the intense vascularity of the hyperplastic intestinal wall, and steroids occasionally reduce the bleeding by decreasing the tissue hyperplasia and perhaps by decreasing vascular permeability. Excessive friability of the intestinal wall has not been encountered in those patients given steroids and later requiring operation. The incidence and severity of complications during steroid therapy can be reduced by constant, careful clinical and laboratory observations, by the routine prophylactic administration of sulfonamides, and by the prompt correction of anemia, hypoproteinemia, and electrolyte and fluid imbalance. Frequent measurements of the serum electrolytes, erythrocyte and leukocyte counts, blood sugar level, and urine facilitate early recognition and prompt treatment of the various complications. Potassium deficits are corrected by the intravenous administration of 40 to 160 mEq. of potassium chloride daily; orally administered potassium salts are irritating to the intestine in many patients with ulcerative colitis and are not prescribed routinely.

In general, the adrenocortical hormones appear to be useful adjuncts to the comprehensive treatment of ulcerative colitis, acting as "therapeutic bridges," initiating and potentiating the recovery phase, facilitating control of severe recurrences, and providing an opportunity for "total treatment." Their use at present seems to have lowered the mortality and to have decreased the need for surgery. When prescribed with proper supervision and vigilance, the adrenal steroids can be administered with relative safety for long periods to patients with ulcerative colitis. Under steroid therapy rectal strictures decrease or disappear, and the roentgenologic appearance of the colon may improve significantly. Not infrequently, the clinical response is maintained for years after discontinuance of the steroid therapy.

The precise mechanism of action of ACTH and the adrenal steroids is not known. There is no evidence of direct pituitary or adrenal dysfunction in ulcerative colitis and the fundamental character of the disease apparently is not altered permanently by corticoid therapy. As in other illnesses, the steroids reduce the vascular and tissue responses to inflammation and suppress the accompanying toxic reaction. Perhaps they also influence some type of hypersensitivity mechanism in ulcerative colitis or inhibit the production of bacterial endotoxin within the colon. Their ultimate effect on the course of the disease and on the fundamental disease process remains to be determined.

Miscellaneous Materials

Many drugs and techniques have proved ineffective in the treatment of ulcerative colitis. These include antilysozyme compounds, polyvalent antidysentery serum, bacteriophage, antihistaminics, antithyroid drugs, ascorbic acid, cobra venom, enemas containing chemicals such as chloroazodin (Azochloramid), tannic acid, acriflavine, and silver nitrate, parathyroid extract, intracolonic administration of oxygen, hydrochloric acid, insulin, isoniazid, liver extract, epinephrine, posterior pituitary injection (Pituitrin), mucin, rutin, and salicylates. Enemas containing cod liver oil or aluminum hydroxide and kaolin may provide symptomatic relief in mild colitis but they do not influence the disease significantly. Psyllium hydrophilic mucilloid (Metamucil), by absorbing excessive fluid from the feces, may produce a more formed bowel movement. The combination powder of bismuth subcarbonate, calcium carbonate, and calcium phosphate, in equal doses of 1.3 Gm. each, is prescribed occasionally for a similar purpose. Elimination diets have not proved especially helpful, in my experience. The clinical effect of various vaccines probably is analogous to the "non-specific protein shock" produced by typhoid vaccine, artificial fever, or foreign protein. There appears to be no satisfactory rationale for the administration of acid-alcohol extracts of intestinal mucosa from hogs in ulcerative colitis. The use of antiamebic drugs for presumptive amebic infections is ineffective in ulcerative colitis and often increases the abdominal discomfort and the diarrhea.

Surgical Considerations

The frequent recurrences of the disease and the recent improvements in surgical technique have increased interest in the operative treatment of ulcerative colitis.[10] In my experience, surgery is required in 10 to 15% of patients. The absolute indications are perforation of the colon, extensive polyposis, carcinoma, persistent massive hemorrhage, and stricture of the colon with obstruction. Colectomy may be necessary in patients with extensive persistent perirectal infection and fistula formation. Surgery also may be required in patients not responding to comprehensive medical management, including steroids, in the hospital. "Chronic invalidism" and "failure of medical treatment" are highly arbitrary designations, requiring thorough evaluation. Careful analysis often reveals inadequate treatment rather than irreversible disease. Thus, many patients previously advised to undergo surgery have responded satisfactorily to skillful medical management. An outstanding example is that of a young woman with severe colitis, who, in 1934, was advised to undergo an ileostomy. The procedure was delayed by an upper respiratory infection, and during this interval the clinical improvement was so pronounced that operation was postponed indefinitely. The proctoscopic appearance of the intestine gradually returned to normal. Subsequently, there was striking reversibility in the roentgenologic appearance of the colon. The patient remains well nearly 25 years later, without surgical treatment. Similar reversibility of the disease has been noted recently in two patients, one of whom was advised to undergo surgery in 1946 and in both of whom the roentgenologic appearance of the colon now is normal. The decision for operation should not result from frustration with a difficult problem nor should it be determined exclusively by economic considerations, though the financial burden imposed by the illness cannot be ignored.

The increased incidence of carcinoma in patients with ulcerative colitis presents a serious therapeutic dilemma.[11] Surgery often is advised in patients with colitis of 10 or more years' duration, as a preventive measure. However, routine colectomy and ileostomy in young men and women, otherwise in excellent health, seems undesirably radical; careful evaluation of each patient clinically, roentgenologically, and by exfoliative cytological study of colonic washings seems preferable. There is no decisive evidence that inflammatory pseudopolyposis directly predisposes to carcinoma in ulcerative colitis; hence, this situation is not necessarily an indication for operation. Surgery is not indicated for rheumatoid arthritis, anemia, iritis, or pyoderma gangrenosum, except under unusual circumstances, since these complications respond to medical management. Patients with cirrhosis, portal hypertension, and esophageal varices with hemorrhage may undergo portacaval or splenorenal shunts successfully and subsequently maintain satisfactory health without need for colectomy. Surgery is hazardous and usually contraindicated in patients with ileocolitis; the associated steatorrhea may be identified by measurements of the plasma carotene and the excretion of fat in the feces.

When surgery is necessary in ulcerative colitis, the procedure of choice usually is total colectomy and ileostomy performed in one or two stages. Chemotherapy and advances in medical and surgical care, in anesthesia, and in operative technique have reduced the operative mortality significantly. Improvements in the construction of the ileostomy[7] and in ileostomy appliances, and intelligent discussion of the operation with the patient, together with the helpful advice of other ileostomy patients, have greatly facilitated the adjustment to the procedure.

Ileostomy alone does not cure ulcerative colitis. Subtotal resection of the colon and anastomosis of the ileum to the sigmoid or rectum seems possible only in those few patients who are without demonstrable involvement of the rectum. Abdominoperineal resection is necessary when the rectum is severely diseased and the source of recurrent bleeding and infection. In segmental colitis of the cecum, ascending colon, or transverse colon which does not respond to adequate medical treatment, the operative procedure usually is limited resection and restoration of normal intestinal continuity. The procedures of vagotomy and pelvic autonomic neurectomy apparently have not been adopted generally. A unique surgical approach involves electrocoagulation of a small prefrontal area in the brain, attempting to interrupt the connection between the frontal convolutions, the thalamus, and the hypothalamus. The objective presumably is to eliminate cerebral control of the autonomic centers in the diencephalon and to decrease neurogenic stimulation of the intestine; the rationale and the effectiveness of this procedure in ulcerative colitis cannot be evaluated at present.

Surgical treatment often is the only effective method of restoring patients with chronic ulcerative colitis to a useful life; at times, the operation is lifesaving. However, the operative results are not uniformly successful.[12] The possible complications after surgery include bleeding, prolapse, infection, fistula formation, perforation and stenosis of the ileostomy, ulceration of the skin, intestinal obstruction, the development of enteritis, and severe electrolyte and fluid deficiencies. The inadequate intake of food, excessive loss of nitrogen in the feces, and the prolonged administration of large amounts of steroids may cause serious nutritional depletion, delaying wound healing and predisposing to infection. However, the careful use of steroids and prophylactic chemotherapy and adequate nutritional care permit many patients to negotiate the surgical procedure without serious difficulty. In such cases the quantity of steroids is increased temporarily, immediately preceding, during, and after operation (cortisone, 300 mg., or hydrocortisone, 200 mg. intramuscularly or 100 mg. intravenously for 24 hours). The medication can be discontinued gradually during the first two weeks of convalescence, if so desired.

Comment

The chronicity, recurrences, and many complications of ulcerative colitis present a uniquely complex therapeutic problem. Treatment continually is dominated by the critical question as to the potential reversibility of the disease; the answer, not easily given, will determine the choice between medical or surgical management. If the patient responds favorably to medical treatment, will the effect be sustained? Is colitis ever cured or can it be controlled sufficiently to permit an economically self-sufficient, useful life? What constitutes "medical failure"? What are the dangers of chronic invalidism for the adult, retarded growth development for the child, or life-threatening complications for all patients? These problems are less critical in those with mild or moderately severe ulcerative colitis. Individuals with mild, remitting disease respond to conventional therapy with rest, sedation, antispasmodics, diet, vitamins, antibacterial therapy, and the "psychotherapy" provided by the attending physician. Patients with moderate or severe colitis, in addition, may require transfusions of blood and plasma, parenterally given fluids, iron given intramuscularly, and ACTH and the adrenal steroids. Although the disease tends to recur, the response to these treatments often is favorable.

The therapeutic problem is most critical, of course, in patients with fulminating colitis, continuously active colitis, or severe recurrent disease. The differing opinions concerning medical therapy and surgical treatment concern these cases particularly. In this dilemma, the advances in surgical technique seem to offer a most attractive and apparently rational solution. Complete removal of the colon and rectum does indeed "cure" the disease, with highly satisfactory, occasionally dramatic results. Nevertheless, as emphasized previously, surgery does not always solve the problem of the colitis patient; and ileostomy, no matter how effective, is not the ideal solution. The course after operation may be more serious than previously, as in a young man who died from diarrhea with extreme electrolyte depletion and dehydration, a young man who developed recurrent obstruction of the ileostomy and extensive enteritis, terminating in death, or the young woman who, after total colectomy and ileostomy, developed obstruction of the ileostomy, ascending ileitis, volvulus of the small intestine, subdiaphragmatic abscess, an abdominal pseudocyst, iron-deficiency anemia, recurrent intestinal obstruction, perforation of the small intestine, and fatal peritonitis. The vast majority of experienced physicians and surgeons accept the fact that most patients with ulcerative colitis, perhaps 80 to 90%, are capable of responding to thorough medical management, especially if the program emphasizes complete healing of the active disease during prolonged hospitalization, maintenance of general health, identification and resolution of emotional problems, avoidance of dietary or medicinal agents known to precipitate recurrences or aggravate the disease, added precautions during respiratory infections and other intercurrent illness, and avoidance of fatigue, loss of sleep, overwork, and excessive responsibility.

The therapeutic problem, then, is to select the 10 to 15% of patients with irreversible disease or with complications unresponsive to medical measures. This selection should not be arbitrary, for it often is difficult to predict initially the degree of improvement to be anticipated in many patients. Some individuals with apparently hopeless colitis improve dramatically on medical treatment and remain well. Other patients appearing less severely ill initially for some unknown reason fail to respond and ultimately require surgery. Therefore, except in the presence of serious complications, it has seemed more desirable to undertake detailed observation and a "therapeutic test" under careful supervision in the hospital. Patience and unremitting care are indispensable ingredients to the successful medical management of ulcerative colitis. The emphasis should be on total treatment, with utilization of all appropriate measures. The many favorable responses to prolonged medical management and the occasional transitions of diseased intestine to normal emphasize the potential reversibility of ulcerative colitis.[13] A significant corollary of this concept is the expectation that the knowledge from additional clinical studies of the disease, together with laboratory investigations of the problem, eventually will produce more effective treatment of this devastating illness.

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CONGENITAL BRANCHIOGENOUS ANOMALIES

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Persons with congenital anomalies of branchiogenous origin present varied and interesting clinical findings. Occurring about the ears or on the neck, these lesions may appear in some patients only as insignificant, asymptomatic pits and in others as evident cysts or fistulas. Such lesions may be unilateral or bilateral, and they may be associated with other congenital anomalies. In some cases, because of the depth or the partial or complete obstruction of their tracts, or because of secondary infection, they may offer problems in diagnosis and therapy. This paper is a summary of the cases of 21 hospitalized patients with branchiogenous anomalies seen at Walter Reed Army Medical Center from 1950 to 1955.

Branchiogenous anomalies are of interest because of the varying clinical pictures they present after secondary infection or occlusion. Although the diagnosis of a branchiogenous anomaly may be evident, at times, it is difficult to evaluate the depth or extent of the associated tract. The differential diagnosis includes tuberculous and nontuberculous lymphadenitis, other infectious processes, tumors of the carotid, hygroma, dermoid cysts, lipomas, neurofibromas, hemangiomas, and lymphangiomas. Thorough surgical evaluation and competent extirpation should be carried out. Inadequate treatment of these lesions by sclerosing agents, such as phenol, or by incomplete electrosurgical measures often results in partial obliteration of these tracts, with subsequent secondary infection and unnecessary scarring and disfigurement.

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Classification and Development

Classification and Nomenclature.—Various classifications and nomenclatures for lesions of branchiogenous origin have been offered. The two broad groups, based primarily on anatomic location, are as follows: 1. Anomalies which occur in the preauricular areas and are known as preauricular pits, cysts, or fistulas. These have also been called "sinus preauricularis congenita," "branchial fistula in the external ear," "fistula auris congenita," and "helical fistula." [1] 2. Branchiogenous anomalies which occur anterior to the sternocleidomastoid muscle in a general linear arrangement from the mandibles to the manubrium. Clinically, such lesions are usually cysts or fistulas. While either may be present anywhere in this distribution, Ladd and Gross [2] state that cysts are prone to lie higher in the neck than the cutaneous openings of fistulas. This observation has been true in the present series.

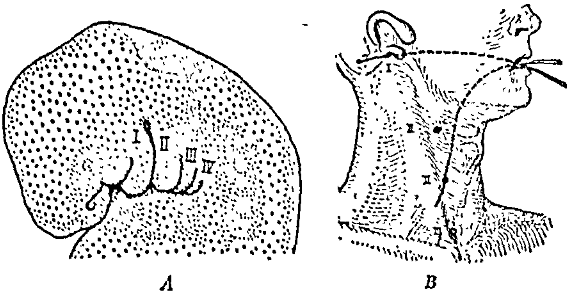

Fig. 1.—*A*, human stages of branchial arches at 5 weeks. *B*, anomalies of branchial apparatus in man showing relationships of cysts and fistulas (published with permission of W. B. Saunders Company).

Again, the nomenclature of these lesions in the neck is not standard; cysts have been known as lateral cervical cysts, lateral cysts of the neck, branchial cysts, and congenital cysts of the neck. Fistulas have been called lateral cervical fistulas, congenital sinuses, and persistent branchial clefts.

Embryology.—Conflicting opinions have been presented regarding the embryologic development of these congenital lesions, and there is no uniformly accepted opinion as to their exact evolution. The following explanation has been presented by Arey [3]: Five branchial arches, separated by four branchial grooves, appear in the fourth week of development of the human embryo (fig. 1*A*). At the level of these external groves, the developing pharynx bulges outward from the entoderm to become the pharyngeal pouches. In the sequence of normal development, the epidermis of each groove and the entoderm of the complementary pouch meet, unite, and finally become obliterated. The anomalies discussed in this paper result from an incomplete obliteration of these grooves during the later developmental cycle.

The auricle develops around the first branchial groove, its tissue being formed by the first and second branchial arches (mandibular and hyoid). During the sixth week, six primitive hillocks appear on these parts. Earlier, it was felt that the auricle developed in a precise manner from these hillocks and from an auricular fold of the hyoid integument. Later studies are controversial; some investigators even assert that the entire auricle, except for the tragus, is of hyoid origin. Anomalous development in this region results in pits or fistulas of varying depth about the ear (fig. 1*B*).

The majority of the more caudad lesions of the neck are said to be derived from the second branchial groove. Various types of lesions result from the residuals of incompletely closed ectodermal grooves or pouches. Fistulas may communicate between the external surfaces of the neck and the pharynx; blind fistulas may lead from the pharynx or, more commonly, from the skin of the neck as a result of a persistent ectodermal groove or entodermal pouch.[3]

Results of Study

Locations of the lesions in this group of 21 patients are shown in figure 2. Lesions occurred in the preauricular areas in seven patients. In four of these, the lesions were bilateral; one had both preauricular pits and fistulas in the neck. In three instances, small preauricular pits were noted only as incidental findings in newborn infants. In the four other patients, all adults, the findings were more significant; mucoid drainage was noted from one tract and purulent exudates from the others. The depth of these tracts was variable; however, in one patient the length was 5 cm. The depth was demonstrated either by diagnostic procedures or by surgical dissection. Operation was performed in three instances. Histological study of the excised material revealed stratified squamous epithelium lining the tract. The underlying rete pegs were normal, and no skin appendages were described. In

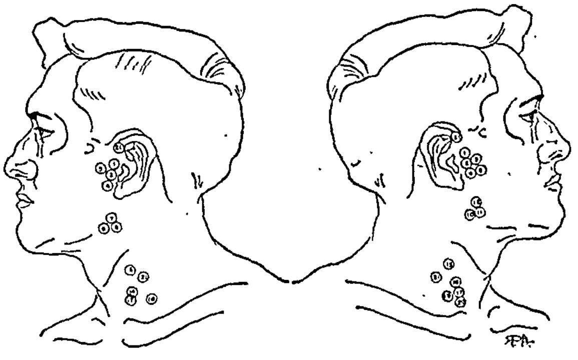

Fig. 2.—Location of congenital branchiogenous lesions in this series of patients.

lying between the external and internal carotid arteries and extending to the palatine tonsil. Histological examination revealed a *sinus tract lined with ciliated columnar epithelium.*

Comment

Branchiogenous anomalies are of interest because of the varying clinical pictures they present after secondary infection or occlusion. In some patients, the drainage from an apparently insignificant orifice may cause pyodermas or infectious eczematoid dermatitis in the surrounding skin. Such lesions may simulate granulomas or carcinomas. Other [illegible]s may become occluded and form cysts which [illegible] become secondarily infected, or, in some in[illegible]es, they may enlarge sufficiently to produce [illegible] symptoms.

Although the diagnosis of a branchiogenous [illegible]omaly may be evident, at times it is difficult [illegible] evaluate the depth or extent of the associated [illegible]ct, which can vary in length from 1 to 10 cm. and occasionally extend as through-and-through (skin-to-pharynx) sinuses. These sinuses may have divergent offshoots and vary in the character of their linings from stratified squamous and columnar epithelium to nonspecific fibrous tracts. In the neck, they often lie in close proximity to important deep structures, such as the carotid vessels and jugular veins.

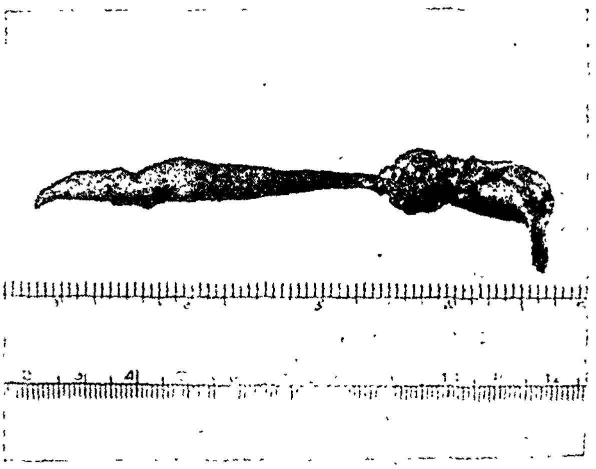

Fig. 7 (case 2).—Dissected fistulous tract.

In their differential diagnoses, Neel and Pember-
[illegible] include tuberculous and nontuberculous
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Adequate diagnostic studies should be carried out to evaluate these lesions prior to treatment. In order to determine their extent, procedures should include careful probing or installation of radiopaque material followed by radiography. It may also be necessary, when attempting dissection, to delineate the tracts with a stain, such as methylthionine chloride (methylene blue).[7] The details of surgical techniques used in the treatment will not be described, but it is important to emphasize that thorough surgical evaluation and competent extirpation should be carried out. Inadequate treatment of these lesions by sclerosing agents, such as phenol, or by incomplete electrosurgical measures often result in partial obliteration of these tracts with subsequent secondary infection and unnecessary scarring and disfigurement.

Summary

Among a group of 21 patients with congenital branchiogenous anomalies studied at Walter Reed Army Hospital from 1950-1955, preauricular pits and fistulas were present in 7; in the other 14 patients, lesions occurred as cysts usually at the angle of the mandible or as fistulas in the lower one-third of the neck. Complications from branchiogenous anomalies result from secondary infection or from pressure. It is necessary to differentiate these lesions by adequate studies from benign and malignant tumors or from chronic infections. When treatment of these lesions is required, thorough surgical extirpation is indicated rather than a method which would result in incomplete obliteration of the tract.

The Medical Illustration Section, Walter Reed Army Hospital, and the Armed Forces Institute of Pathology supplied some of the photographs used in this paper.

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were found in the mid-neck along the medial border of the sternocleidomastoid muscle (fig. 4). A mucoid discharge could be expressed from these areas. Symmetrically placed ostia were also present on the anterior helix of both ears, and there was intermittent drainage from these sinuses. The lesions on the anterior helix and in the neck were diagnosed as multiple congenital branchiogenous anomalies. During the patient's hospitalization the deafness was found to be bilateral and of undetermined origin. Initially, a Maico air-conduction hearing aid was fitted for the left ear in October, 1953, and one month later a contact dermatitis, apparently due to the hearing mold, developed. This was associated with secondary infection of the external ear and of the preauricular sinuses. These complications subsided on symptomatic treatment, and the patient was later discharged.

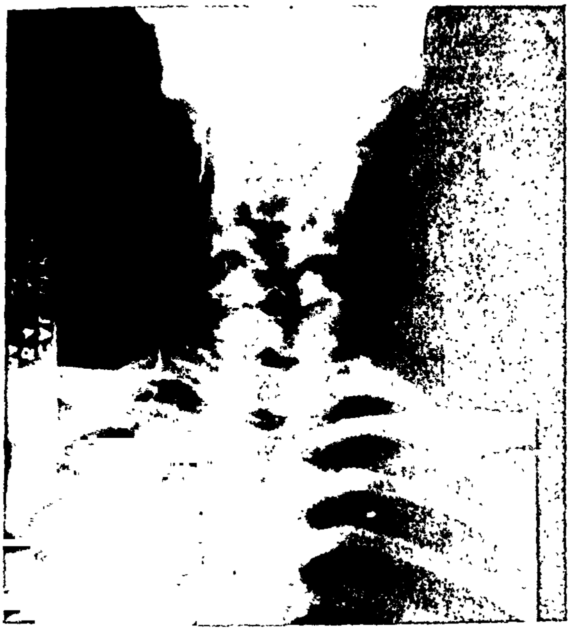

Fig. 5 (case 1).—Roentgenogram with delineation and extent of tract shown by iodized oil (Lipiodol)–filled polyethylene tube.

The patient was readmitted March 12, 1954, with a history of recurrent dermatitis with secondary infection about the ear, apparently due to the hearing mold. The fistulas of the neck were draining, and Staphylococcus pyogenes var. aureus resistant to penicillin but sensitive to other antibiotics was isolated.

Roentgenographic studies of sinus tracts of the neck with use of iodized oil (Lipiodol) revealed a branchiogenous fistula beginning on the level of C-5 on the right, extending slightly medial to the angle of the jaw, and appearing to end at about the base of the neck laterally. A subsequent x-ray of the soft tissues of the neck after catheterization of the sinus on the left showed a polyethylene tube, filled with iodized oil, which extended from the clavicle on the left superiorly with a concentration of the contrast medium extending into the pharynx at the level of C-2 (fig. 5). On June 9, 1954, with the patient under general endotracheal anesthesia, the right tract was surgically excised. This tract was noted to pass in close proximity to the external and internal carotid arteries anteriorly and was followed to the pharyngeal wall. The left tract was removed from a similar area. After operation, hemorrhage developed about the wound in the neck, which resulted in respiratory difficulties with laryngospasm. This was sufficiently severe to require a tracheotomy on June 10, at which time a large clot of blood was evacuated from the wound. After this procedure, the patient made a gradual but uneventful recovery.

Pathological studies of the dissected tracts revealed tubular structures which were lined, in some portions, with stratified squamous epithelium and, in other areas, by pseudostratified ciliated columnar epithelium. The surrounding tissue was densely infiltrated with lymphocytes to form lymphoid aggregates.

Prior to the patient's discharge on Sept. 17, 1954, hearing molds, made of another plastic material so that wearing could be alternated, were fitted to each ear of this patient.

Case 2.—A 22-year-old man (fig. 2, no. 20) was admitted on Jan. 25, 1952, with a sinus, on the right side of his neck, which had been draining purulent material intermittently for as long as he could remember. There was no family history of similar lesions.

Examination showed a small elevation on the right side of the base of the neck with a central opening and mucopurulent drainage. This orifice communicated with a palpable sac extending upward on the right side. This appeared adherent to the deeper structures above, since it retracted when the patient swallowed. The thyroid gland was not palpable. To determine the depth of the tract, iodized oil was instilled and roentgenograms were made (fig. 6). These demonstrated that the tract extended from the right supraclavicular area at the level of D-2 to the level of C-3. The inferior end communicated with an ovoid cystic structure located superficially in the anterior portion of the neck at the level of D-1 or D-2. A diagnosis of branchiogenous sinus was made.

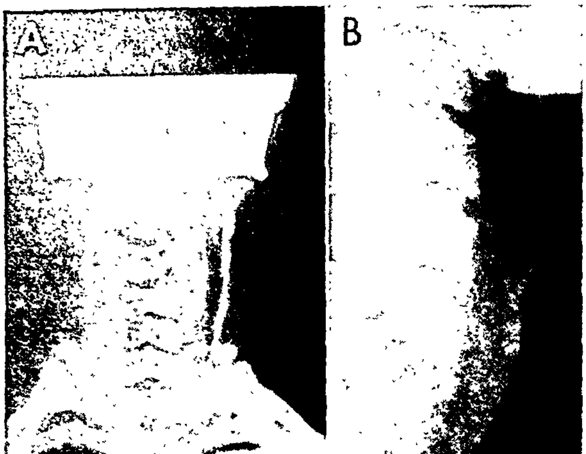

Fig. 6 (case 2).—Roentgenograms showing iodized oil (Lipiodol)–filled tract: *A*, anteroposterior view and, *B*, lateral view.

In February, 1952, with the patient under general endotracheal anesthesia, the entire fistula was dissected (fig. 7). It was shown to extend for a distance of approximately 7 cm., one specimen the dermis was infiltrated with neutrophils with an infiltrate of plasma cells and lymphocytes at the periphery.

Lesions in the neck were present in 14 other patients. The two clinical types seen were (1) those evidenced as firm, freely movable cysts and (2) those with openings on the skin of the neck with associated fistulous tracts.

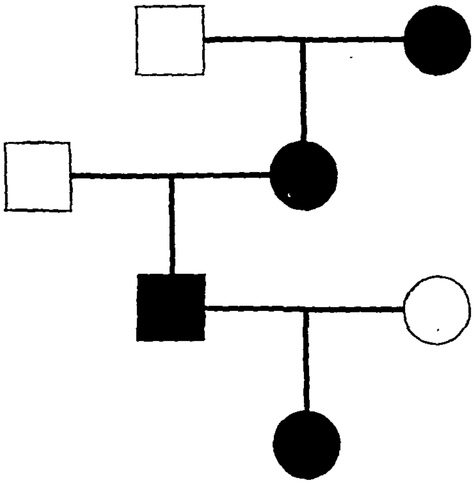

Fig. 3.—Diagrammatic history of family with branchiogenous anomalies of lower neck, showing evidence in three generations.

Cystic lesions in the neck were observed in seven patients. All of these occurred at the angle of the mandible, except in the patient in case 18, in whom the tumor was located just above the midthird of the clavicle. The cystic structures were unilateral, freely movable, and nontender, and they varied in diameter up to 5 cm. In one patient, rapid growth of the mass was noted, and various diagnoses, including parotid tumor, lymphatic tumor, and aberrant thyroid gland, had been entertained. In five patients the cysts were surgically excised, and histological examination showed stratified squamous epithelium lining the cysts and lymphoid tissue which contained well-defined germinal centers.

There were fistulous lesions with openings in the neck in the other eight patients, with only two showing bilateral orifices. These lesions tended to be present in the lower third of the neck. The orifices varied in appearance from small asymptomatic pinpoint openings to an inflamed, tender, swollen mass which, in one patient, suggested a furuncle; hyperpigmentation about the ostia was common. Drainage was mucoid in two and frankly purulent in six patients. Periodic drainage was described by three patients in whom symptoms of tenderness and pressure were relieved when the tracts were evacuated.

Surgical excision of the tracts was performed in six patients. These tracts were often in close proximity to major deep neck structures, such as the carotid arteries and jugular veins, and required careful dissection for their removal. In two instances the tracts, after complete dissection, were shown to terminate adjacent to the pharynx; in one, a pharyngeal opening was demonstrated.

In summarizing associated anomalies in this group of 21 patients, one individual had both bilateral preauricular pits and sinuses in the neck and was the only patient showing multiple branchiogenous anomalies at several levels. Among those patients with preauricular lesions, other anomalies noted were multiple hemangiomas of the hand and forearm in one newborn infant, a deformed auricle in one, and bilateral perceptive deafness in three. While several reports confirm the presence of heredity factors in preauricular lesions, none was noted in our group. In the group of 14 patients with branchiogenous anomalies in the neck, however, 3 gave a family history of this condition occurring over several generations. The diagnostic history of one family is presented in figure 3. No other anomalies were observed in this group.

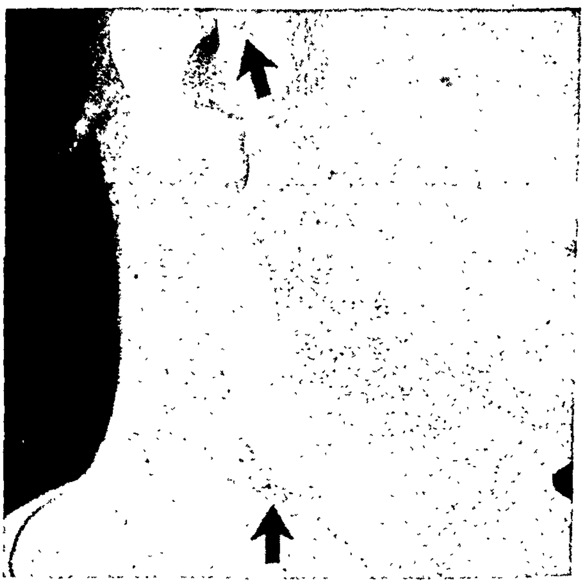

Fig. 4 (case 1).—Branchiogenous anomaly with sinuses in lower neck and pits anterior to helix.

Report of Cases

Case 1.—A 21-year-old man was admitted to Walter Reed Army Hospital on Sept. 23, 1953, with a complaint of partial deafness which had existed since birth (fig. 2, no. 21). He also described repeated troublesome infections occurring in small sinuses in his mid-neck. A family history of deafness in the patient's father and paternal grandfather was given, and there was a history of "cysts of the neck for several generations." On examination, two symmetrical draining sinuses were found in the mid-neck along the medial border of the sternocleidomastoid muscle (fig. 4). A mucoid discharge could be expressed from these areas. Symmetrically placed ostia were also present on the anterior helix of both ears, and there was intermittent drainage from these sinuses. The lesions on the anterior helix and in the neck were diagnosed as multiple congenital branchiogenous anomalies. During the patient's hospitalization the deafness was found to be bilateral and of undetermined origin. Initially, a Maico air-conduction hearing aid was fitted for the left ear in October, 1953, and one month later a contact dermatitis, apparently due to the hearing mold, developed. This was associated with secondary infection of the external ear and of the preauricular sinuses. These complications subsided on symptomatic treatment, and the patient was later discharged.

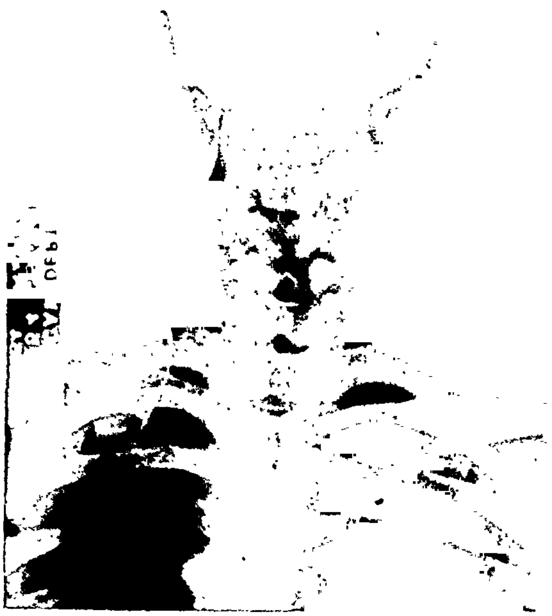

Fig. 5 (case 1).—Roentgenogram with delineation and extent of tract shown by iodized oil (Lipiodol)-filled polyethylene tube.

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Examination showed a small elevation on the right side of the base of the neck with a central opening and mucopurulent drainage. This orifice communicated with a palpable sac extending upward on the right side. This appeared adherent to the deeper structures above, since it retracted when the patient swallowed. The thyroid gland was not palpable. To determine the depth of the tract, iodized oil was instilled and roentgenograms were made (fig. 6). These demonstrated that the tract extended from the right supraclavicular area at the level of D-2 to the level of C-3. The inferior end communicated with an ovoid cystic structure located superficially in the anterior portion of the neck at the level of D-1 or D-2. A diagnosis of branchiogenous sinus was made.

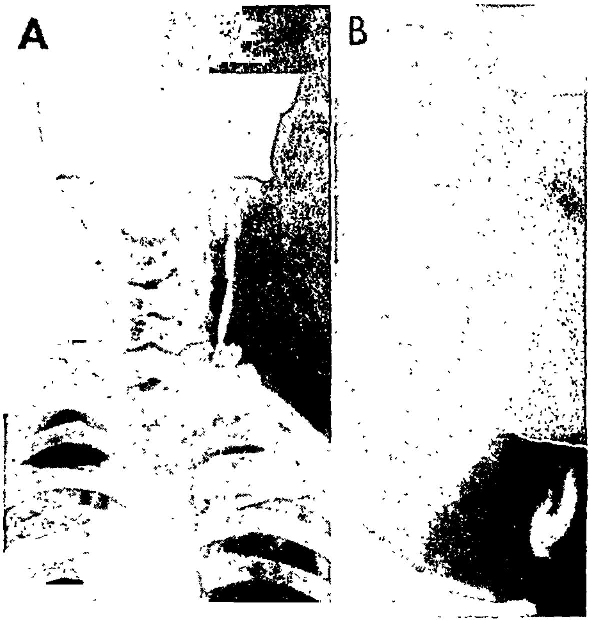

Fig. 6 (case 2).—Roentgenograms showing iodized oil (Lipiodol)-filled tract: *A*, anteroposterior view and, *B*, lateral view.

In February, 1952, with the patient under general endotracheal anesthesia, the entire fistula was dissected (fig. 7). It was shown to extend for a distance of approximately 7 cm., lying between the external and internal carotid arteries and extending to the palatine tonsil. Histological examination revealed a sinus tract lined with ciliated columnar epithelium.

Comment

Branchiogenous anomalies are of interest because of the varying clinical pictures they present after secondary infection or occlusion. In some patients, the drainage from an apparently insignificant orifice may cause pyodermas or infectious eczematoid dermatitis in the surrounding skin. Such lesions may simulate granulomas or carcinomas. Other fistulas may become occluded and form cysts which may become secondarily infected, or, in some instances, they may enlarge sufficiently to produce pressure symptoms.

Although the diagnosis of a branchiogenous anomaly may be evident, at times it is difficult to evaluate the depth or extent of the associated tract, which can vary in length from 1 to 10 cm. and occasionally extend as through-and-through (skin-to-pharynx) sinuses. These sinuses may have divergent offshoots and vary in the character of their linings from stratified squamous and columnar epithelium to nonspecific fibrous tracts. In the neck, they often lie in close proximity to important deep structures, such as the carotid vessels and jugular veins.

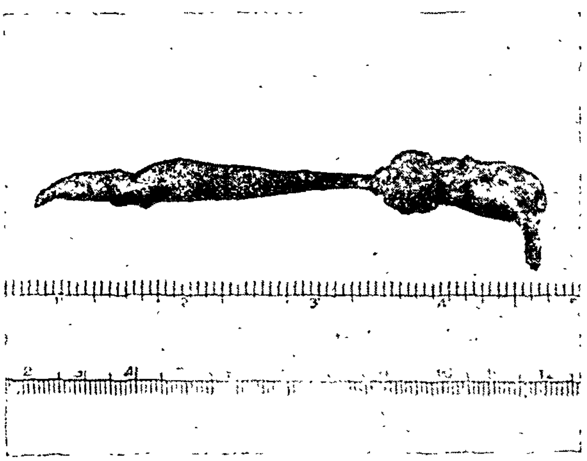
Fig. 7 (case 2).—Dissected fistulous tract.

In their differential diagnoses, Neel and Pemberton[4] include tuberculous and nontuberculous lymphadenitis, other infectious processes, tumors of the carotid, hygroma, dermoid cysts, lipomas, neurofibromas, hemanginomas, and lymphangiomas.

The association of branchiogenous anomalies with other congenital anomalies noted in this reported series has been observed previously by other authors,[5] as has the hereditary history obtained in some cases.[6]

Adequate diagnostic studies should be carried out to evaluate these lesions prior to treatment. In order to determine their extent, procedures should include careful probing or installation of radiopaque material followed by radiography. It may also be necessary, when attempting dissection, to delineate the tracts with a stain, such as methylthionine chloride (methylene blue).[7] The details of surgical techniques used in the treatment will not be described, but it is important to emphasize that thorough surgical evaluation and competent extirpation should be carried out. Inadequate treatment of these lesions by sclerosing agents, such as phenol, or by incomplete electrosurgical measures often result in partial obliteration of these tracts with subsequent secondary infection and unnecessary scarring and disfigurement.

Summary

Among a group of 21 patients with congenital branchiogenous anomalies studied at Walter Reed Army Hospital from 1950-1955, preauricular pits and fistulas were present in 7; in the other 14 patients, lesions occurred as cysts usually at the angle of the mandible or as fistulas in the lower one-third of the neck. Complications from branchiogenous anomalies result from secondary infection or from pressure. It is necessary to differentiate these lesions by adequate studies from benign and malignant tumors or from chronic infections. When treatment of these lesions is required, thorough surgical extirpation is indicated rather than a method which would result in incomplete obliteration of the tract.

The Medical Illustration Section, Walter Reed Army Hospital, and the Armed Forces Institute of Pathology supplied some of the photographs used in this paper.

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RADIATION THERAPY FOR STOMA ULCER OCCURRING AFTER SUBTOTAL GASTRECTOMY

Everett D. Kiefer, M.D.
and
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The effectiveness of roentgen radiation in depressing or abolishing glandular secretion can be turned to account in producing achlorhydria for therapeutic purposes. Duodenal ulcers occurring opposite the stoma after Billroth 2 operations were studied in 23 patients. In order to reduce the secretion of acid by the gastric remnant, it was irradiated, generally with supervoltage x-rays (2 mev.). The tissue dose was approximately 1,800 r in all cases. The resulting reduction in gastric acidity was variable and unpredictable, but analyses showed that achlorhydria or pronounced hypochlorhydria was present in more than half of the patients up to two years after irradiation. Clinically satisfactory results were obtained in 15 patients after one course of therapy. Experience indicated that patients in whom the achlorhydria persisted for three years were unlikely to have further ulceration or to need additional surgery.

In the surgical treatment of duodenal ulcer, any operation which joins gastric mucosa to the mucosa of the small intestine may be followed in an appreciable proportion of cases by an anastomotic ulcer; subtotal gastrectomy provides no exception to this rule.

Although it is generally accepted that subtotal gastrectomy with use of a Billroth 2 type of anastomosis has resulted in a lower incidence of recurrent ulcer than the Billroth 1 resection, hemigastrectomy, or gastroenterostomy, the number of stoma ulcers occurring after high resection is large enough to be significant. In a 10-year follow-up study of 351 consecutive patients with duodenal ulcer who were subjected to the Billroth 2 subtotal gastrectomy, anastomotic ulcers developed in 6.6%.[1]

Stoma ulcer occurring after operation is a serious clinical development which usually presents a much more difficult therapeutic problem than the primary duodenal ulcer. Conventional medical treatment with antacids and anticholinergic drugs may relieve symptoms as long as the patient is at rest, but when normal activity is resumed symptoms and signs of active ulceration are likely to recur.

Evidence that the surgical treatment of gastrojejunal ulcer is not satisfactory may be found in the report of Walters and associates.[2] In patients with recurrent jejunal ulcer after gastric resection, vagotomy produced achlorhydria in only one-half and the clinical results were unsatisfactory in 30%. Resection of the anastomosis and a portion of the remaining gastric stump combined with a subdiaphragmatic vagotomy appeared to give the best surgical results. However, this is a formidable procedure to recommend to a patient who has already gone through a major operation for relief of ulcer, and any further reduction of the size of the gastric stump may prove to be a serious handicap to the patient's nutrition after a second operation.

There is clinical evidence that the postoperative development of a stoma ulcer is in itself an indication that the ulcer diathesis in the patient is so strong that peptic ulceration will occur unless a sustained and complete achlorhydria has been achieved. In patients who were subjected to resection for stoma ulcer occurring after a previous operation, a second stoma ulcer developed in 14.5%—more than twice the incidence observed in patients operated on for duodenal ulcer.[1] Cases have been reported in which ulcers recurred after all but a tiny remnant of stomach had been removed, but most clinicians will agree that total gastrectomy is too radical a surgical procedure for a benign condition. It is generally agreed that postoperative ulceration is dependent on the persistence of free hydrochloric acid in the secretions of the gastric stump, and all therapeutic plans have as their objective either the neutralization or the elimination of the acid factor.

The idea of using radiation in a deliberate attempt to produce gastritis and thereby reduce gastric secretion in cases of duodenal ulcer was first suggested in 1909 by Bassler.[3] Bruegel[4] in 1917 and Holman and Lewis[5] in 1941 reported on the use of irradiation of the stomach in the treatment of duodenal ulcer. During the last 10 years several studies have been made on the value of gastric irradiation in the treatment of peptic ulcer.[6]

The amount of radiation generally used has ranged from 1,600 to 2,000 r delivered into the stomach. The reduction in gastric acidity produced by these dosages is variable and unpredictable, but

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as a rule the acidity begins to diminish in two to four weeks after irradiation, continues to decrease for several weeks or months, and then tends to return gradually to the same level as before treatment. Achlorhydria develops in about 12% of patients but may be transient. In the majority of patients, pretreatment levels of acid secretion have been resumed in about two years.

By gastroscopic and serial biopsy methods, the degree of inflammation of the gastric mucosa has been shown to parallel the effect on secretion.[7] Acute irradiation gastritis develops, reaches a peak of severity, and then subsides—the mucosa in most cases returning to normal without fibrosis. In a few instances, some atrophy persists and prolonged hypochlorhydria or achlorhydria then is usually present. Although present evaluations indicate that irradiation therapy is best considered as an adjunct to conventional treatment of duodenal and gastric ulcer, it may well be more applicable in the management of stoma ulcer after subtotal gastrectomy.

Clinical Material and Methods

Clinical Material.—This report is based on our experience with the use of supervoltage x-ray therapy in 23 patients with stoma ulcer after subtotal gastrectomy. Since the series is small and the follow-up period less than two years in the majority of cases, this paper must be considered a preliminary report. Further long-term observations are necessary for final evaluation of the method.

Only 1 of the 23 patients was a woman. Twelve had undergone gastric resection at the Lahey Clinic, and 11 had been operated on elsewhere. In every case gastric resection with a Billroth 2 type of anastomosis had been used, and in only one did x-ray examination indicate that less than 70% of the stomach had been removed. In seven cases the gastric resection had been carried out in an attempt to cure a stoma ulcer which had occurred after a previous operation. In four cases vagotomy had been performed. Eight patients had been hospitalized for a trial of medical treatment which was unsuccessful.

Diagnosis.—In 18 of the 23 patients an ulcer crater on the jejunal side of the anastomosis was demonstrated by x-ray examination. In the remaining five, the only objective evidence of ulcer was hemorrhage from the gastrojejunal area. Free hydrochloric acid was demonstrated in the gastric secretions before treatment in all but one patient, and in this patient only one examination was made. Inherent difficulties in gastric analyses after gastric resection make repeated tests necessary to determine the true level of secretion. A high level of free acid may be considered extremely significant in the diagnosis of recurrent ulcer.

Our method of obtaining gastric juice from the resected stomach was to keep the patient lying flat in the supine position with the tip of a Levin tube in the fundus. A fractional analysis was made with use of either Ewald's test meal or histamine as a stimulant. The sample showing the highest titer of acidity was considered to be the significant specimen. A high level of acid secretion by the gastric remnant was the rule in the 18 patients in whom a crater was demonstrated by x-ray; the free acidity was 20 degrees or over in 12 and 40 degrees or over in 5. In the five patients without demonstrable crater the free acidity was 20 degrees or over in two.

Technique of Irradiation.—Of the 23 patients, 2 were treated by Dr. Joseph Marks at the New England Deaconess Hospital, Boston. One of these was given a second series of treatments at the Massachusetts Institute of Technology three months later. Dr. Marks used 2 mv. of x-ray and the same essential technique as was used by us. Three patients were treated with 400 kv. of x-ray, half-value layer 3.8 mm. Cu, in our radiology department at the Lahey Clinic. All the other treatments were carried out at the Massachusetts Institute of Technology, with 2 mv. of x-ray, half-value layer 12.8 mm. Cu at a target midplane distance of 125 cm. This was part of the cooperative program between the Lahey Clinic and Professor John G. Trump and his associates.

The tissue dose was approximately 1,800 r in all cases. The three patients treated at the clinic with 400 kv. of x-ray received approximately 1,700 r. The plan of therapy is to give a tissue dose of 180 r five times weekly for two weeks, or 10 treatments. Anterior and posterior fields are used on alternate days. The patients are in a standing position, and, since we wish to treat only the gastric stump, field sizes usually do not have to be larger than 10 by 10 cm. provided the localization is accurate. We consider the localization of portals highly important, and in our opinion one of the prime factors in producing poor results after x-ray therapy is lack of proper localization of the x-ray beam.

Results

Acid Secretion.—Because most of these patients lived some distance from Boston, it was impossible to check the gastric acidity at regular fixed intervals. In all but four, however, gastric analyses were made at irregular intervals after treatment. Altogether, 42 gastric analyses were carried out on 19 patients during the first two years after treatment. There was one during the third year and one during the fourth year. In all but one instance, the free acid titer was well below the free acid figure in that patient before irradiation. The tabulated results (see table) show that achlorhydria or pronounced hypochlorhydria was present in over one-half of the patients up to two years after irradiation.

In 10 patients tested within the first two months after x-ray therapy, the level of free acid was found to be reduced in comparison with the pretreatment figure. The free hydrochloric acid level was 5 units or less in three patients, and in three achlorhydria was present. In 12 patients tested during the following four months (the period from two to six months after therapy), the free acid level was reduced in all but one. It was less than 5 units in one, and achlorhydria was present in five. In 10 patients tested during the second six-month period after therapy, the free acid level was reduced below the pretreatment level in all. Achlorhydria was present in five; three patients had 10 units, and two had 25 units of free hydrochloric acid. In 10 patients tested during the second year after irradiation the free hydrochloric acid level was well below the pretreatment level in all. Two patients had less than 5 units, and achlorhydria was present in six.

Gastric Stump Acidity After Radiation Therapy

	Period After Therapy, Mo.			
	2	2-6	6-12	12-24
Not tested, no.	10	12	10	10
Free HCl below pretreatment level, no.	10	11	10	10
Less than 5 units of free HCl, no.	3	1	0	2
Achlorhydria, no.	3	5	5	6

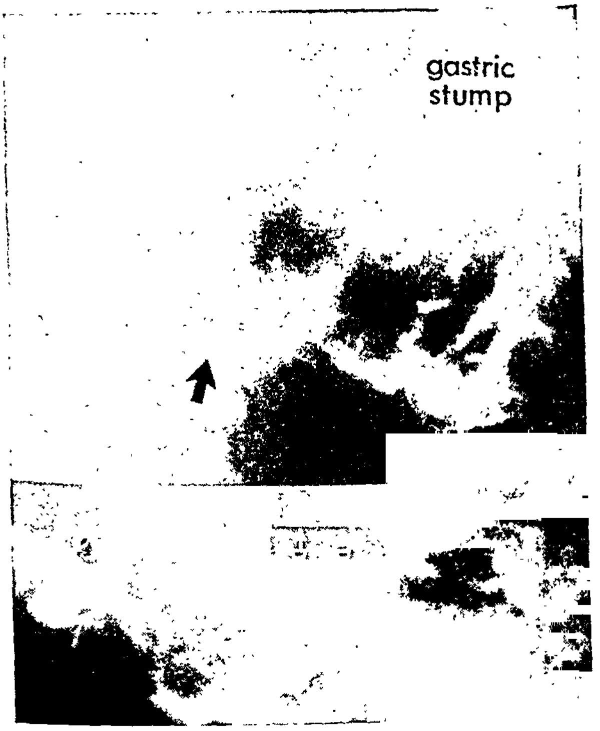

Fig. 1.—Roentgenogram of anastomosis between gastric stump and jejunum, showing ulcer crater (*arrow*) in jejunum just distal to stoma. *Insert*, spot view of stoma and crater.

The results obtained in this small group of patients give some hopeful indication that the recovery of acid-secreting power of the fundal stump is not as likely to occur as it is in the case of the irradiated intact stomach and that, if achlorhydria or nearly complete achlorhydria is once established, it may persist.

Ulcer Crater as Visualized by X-ray.—In 18 of the 23 patients, the pretreatment diagnostic evidence included the demonstration of an anastomotic crater by x-ray. In 12, diagnostic x-ray studies after treatment showed that the crater had healed. In two others the crater disappeared only after a second course of irradiation treatment. Two patients lived too far away to return for follow-up x-ray studies but reported that they were symptom-free one and one-half and eight years, respectively, after treatment. In the two remaining patients, craters were found 34 and 36 months after treatment. Both of these patients had been symptom-free for almost three years, which would suggest that the primary crater had initially healed but subsequently recurred.

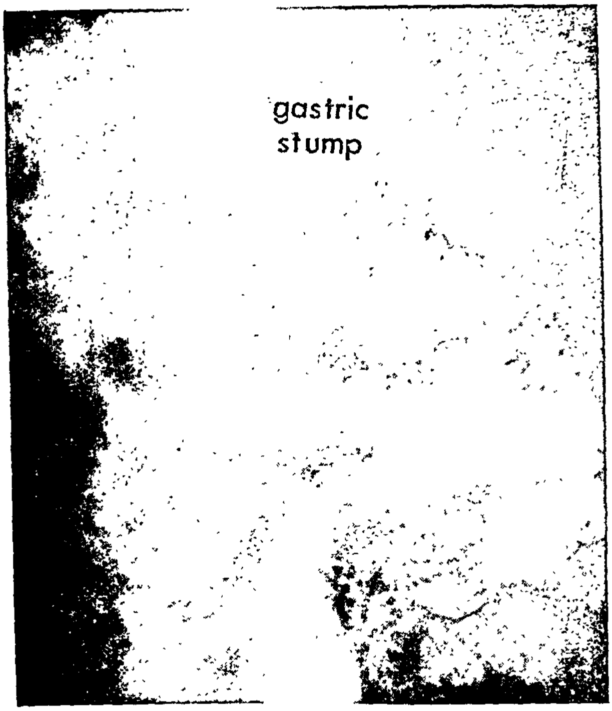

Fig. 2.—Roentgenogram of anastomosis between gastric stump and jejunum four months after irradiation therapy, showing smaller mucosal folds and no ulcer crater.

In some instances a post-treatment x-ray examination carried out less than two months after irradiation showed that the crater was still present but reduced in size; these craters subsequently disappeared. Figures 1 and 2 show x-ray evidence of the healing of a stoma ulcer after irradiation of the gastric stump. The observations on 18 patients in whom anastomotic craters were demonstrated before treatment indicate that these craters consistently heal if gastric acidity is abolished by one, two, or three courses of irradiation therapy. If the acid secretory power is recovered by the gastric stump, however, a new crater may form.

Hemorrhage But No Demonstrable Crater.—Five patients were treated for recurrent hemorrhage after subtotal gastrectomy. They had persistently high levels of acid secretion but no demonstrable ulcer crater. In three of these cases the hemorrhages were multiple. In one patient with an 8-month follow-up study and two with 15-month follow-up studies, achlorhydria was produced and no symptoms have been reported. In one, achlorhydria was not achieved and further hemorrhages occurred until a second course of irradiation was given. Although no further hemorrhage has occurred in the fifth patient, a second course of therapy was given because of persistent acid secretion and some distress.

Relief of Pain.—In 17 of the 23 patients, pain was a prominent symptom before therapy. Pain was relieved in all but three by one course of irradiation. Two of these three patients with persistent pain were eventually relieved after a second course. In one patient, complicating pancreatitis caused pain which persisted for three months after therapy.

Recurrence.—Of the 23 patients treated, 16 have had a follow-up period of less than two years. Eleven of these are still symptom-free and show no evidence of recurrence after one course of therapy. One patient had a recurrent or persistent crater, and hemorrhage occurred in one, and mild pain in another. Further irradiation was given in all three of these patients, and they are now symptom-free. The two remaining patients have died of intercurrent disease.

Seven patients have had follow-up periods of two to eight years. Four of these have remained symptom-free, and in all four the free hydrochloric acid level in the gastric secretions is either absent or very low. In the remaining three, recurrent hemorrhage, pain, and crater formation have occurred from three to five years after therapy. Thus, the present status is satisfactory after one course of therapy in 15, satisfactory after two or three courses in 3, and unsatisfactory because of recurrence in 3. Two died from intercurrent disease.

Side-effects.—No important side-effects were observed in this group, even though two courses of treatment were given in three cases and three courses in one. Four patients complained of some nausea during the treatment. Epilation was noted in one patient, and slight erythema has been observed in several. In one patient who was treated for multiple hemorrhages, some bleeding occurred during the treatment.

No definite evidence of any injury to other organs in the treated area has been noted. Diabetes developed a few months after treatment in one patient, but there was evidence of pancreatitis before therapy. One patient was subjected to left nephrectomy for renal cell carcinoma two years after receiving two courses of irradiation; he later died of metastases. The relationship between the radiation therapy and the subsequent development of carcinoma of the left kidney is a matter for conjecture.

Summary and Conclusions

In 23 patients treated with irradiation, clinically satisfactory results were obtained in 15 after one course of therapy. The results in three other patients were clinically satisfactory after a second or third course of irradiation. In three patients, results must be classified as failure because of recurrence of stoma ulceration, but in all three the supervision was inadequate and there was no opportunity to repeat or supplement the treatment before severe signs and symptoms developed. Two patients died of intercurrent and unrelated disease.

Radiation doses of 1,800 r with 2 mv. of x-ray can be administered to the stump of the resected stomach and, if necessary, repeated one or two times at intervals of six months without serious danger or untoward side-effects. Adequate radiation therapy materially and consistently reduces the secretion of hydrochloric acid, and, if achlorhydria is established, relief of pain and healing of the anastomotic ulcer occur.

Because the suppression of gastric secretion is not always complete or permanent, follow-up studies should be carried out in patients receiving this form of therapy and examinations made for recurrent ulcer or acid secretion; further treatment should be instituted if either condition is found. There is evidence that, if achlorhydria persists for three years after treatment, no further ulceration is to be expected.

In patients with anastomotic ulcer or gastric hemorrhage associated with persistent secretion of gastric acid occurring after subtotal gastrectomy for duodenal ulcer, irradiation of the gastric stump is a safe, rational, and effective treatment which may obviate the need for additional major surgery.

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The Massachusetts Institute of Technology supplied the 2 million-volt radiation sources and assumed responsibility for physical aspects in this study.

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ETIOLOGY OF DUODENAL ULCER

II. SERUM PEPSINOGEN AND PEPTIC ULCER IN INDUCTEES

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The possibility that the concentration of pepsinogen in the blood serum might be correlated with other measurable structural or functional characteristics was investigated in 2,262 men selected randomly at a large army induction center. Pepsinogen values were expressed as micrograms of tyrosine released by the action of 1 ml. of serum in a standard assay procedure. The mean value for 2,031 of these men was 440 units, with a standard deviation of 136. Duodenal ulcer was found in 13 men and gastric ulcer in 1; the mean pepsinogen value for the 14 men was 707 and was significantly higher than that of the group as a whole. A low positive correlation was found between the pepsinogen value and a man's position in his family in that the average value for oldest children was higher than the corresponding figures for younger or only children, but there was no significant correlation with objective measures of social behavior or over-all military performance.

The findings described in this paper are the result of a project begun in October, 1954, by the department of psychiatry at the Walter Reed Army Institute of Research. It was designed to study the development of peptic ulcer in inductees and was conducted initially at a large induction station in the eastern United States. A total of 2,262 randomly selected inductees were chosen for this study over a two-month period at the rate of approximately 300 per week, certain tests and desired items of information being made part of the routine induction procedure. A previous article by Weiner and coworkers [1] reported on some of the initial findings of this project concerning the relationship between psychological characteristics and serum pepsinogen.

The present paper presents a part of the data which have been obtained from a two-year follow-up study of the military performance and medical records of the subjects of this investigation.

A correlation between peptic ulcer and pepsinogen (both serum pepsinogen levels and uropepsin excretion) [2] and between peptic ulcer and ABO blood groups [3] has been demonstrated by current research. Consequently, among the tests chosen for this study were the pepsinogen concentration in the serum and the blood type. In addition, the Cornell Medical Index (CMI), the Saslow test, an extensive, specially designed sociological questionnaire, and photographs for analysis of the somatotypes (Sheldon) were employed. In this paper, certain sociological background data and parts of the CMI are used but the bulk of the material will be reported in separate studies later. The pepsinogen

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values were determined by the method described in the earlier paper.[1] Those individuals whose pepsinogen levels were in the upper and lower 10% of the group each week were specially coded, and a random group of these men (121 subjects, 64 with hypersecretion and 57 with hyposecretion) was selected for additional studies, such as psychological testing, interviews by psychiatrists and psychiatric social workers, and x-rays of the upper gastrointestinal tract. These x-rays were done at the time of induction, again about three or four months later, and, in 97% of the cases, again about a year after induction. The x-ray studies were conducted with special care by well-trained radiologists who were on duty in the large Army hospitals which gave diagnostic and medical service to the troops in the geographical areas to which the subjects of this study were assigned. Clearly, no method is perfect, and, hence, errors—chiefly of omission—have probably occurred. It may be noted, however, that in one subject in whom the first fluoroscopy was suggestive of ulcer, due to spasm, a total of five roentgenographic examinations were conducted with a final diagnosis of "no ulcer." When the data from the various technical studies were compared at the conclusion of the study, it was found that this man had a low serum pepsinogen level—namely, 222 units (expressed as micrograms of tyrosine released by the action of 1 ml. of serum at pH 1.5 in the standard assay procedure[4]), which is in the hyposecretion group.

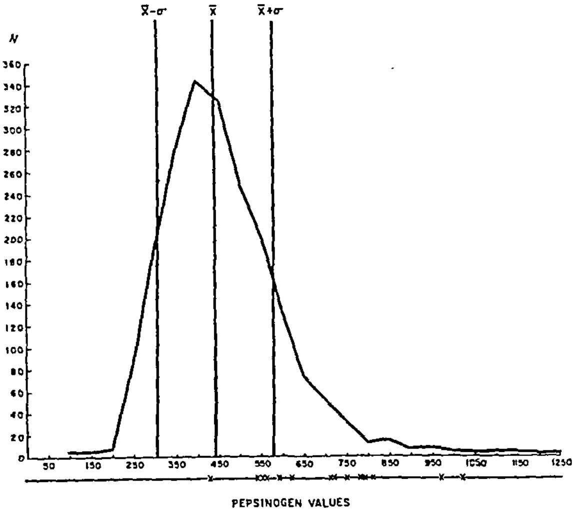

Fig. 1.—Pepsinogen level distribution curve of 2,031 subjects. Mean ($\bar{x}$) = 440; standard deviation (σ) = 136. One standard deviation above mean ($\bar{x} + \sigma$) = 557 = hypersecretion cut-off level; one standard deviation below mean ($\bar{x} - \sigma$) = 304 = hyposecretion cut-off level. Each ulcer case (X) is plotted at pepsinogen level below abscissa.

No attempt was made to influence the assignment of any of the subjects in the total research sample. At the end of one year's service, information was requested from each of the 2,262 men's commanding officers as to their adjustment to military life. At the end of their two years' obligatory service, complete military records, medical as well as administrative, were obtained for each man. Consequently, we were in a position to estimate and evaluate the over-all performance and certain particular incidents for each subject during his military service. Because our population sample was composed of draft-age men, the mean age was correspondingly low—20.8 years; 96% of the group were Caucasian and 3.5% Negro. Only the aspects of this project which deal with pepsinogen, peptic ulcer, and blood groups will be reported in this paper.

Distribution of Pepsinogen Levels and Peptic Ulcer

Although the total research sample was composed of 2,262 men, pepsinogen levels were obtained on only 2,031 subjects because of unavoidable accidents, such as some samples being lost or broken in transit. The distribution of the concentration of pepsinogen in the serum of the 2,031 men is depicted in figure 1. The values ranged from 66 to 1,244 units, with a mean ($\bar{x}$) of 440 and a standard deviation (σ) of 136. Hyposecretion was defined as a pepsinogen value less than one standard deviation below the mean (i. e., 304 or below); hypersecretion was a pepsinogen value greater than one standard deviation above the mean (i. e., 577 and above).

Out of the total research population of 2,262 men, a diagnosis of peptic ulcer was made in 16. However, in two of these subjects pepsinogen values were not obtainable. Therefore, in the sample of 2,031 men, 14 cases of peptic ulcer were diagnosed during the subjects' two-year tours of duty; 13 persons had duodenal and 1 had gastric ulcer. The diagnosis of ulcer was made only if there was positive x-ray evidence of an ulcer crater or scarring secondary to an ulcer. Those with severe pylorospasm were not included.

It is to be noted that eight of the ulcer cases were discovered in the "special study group" of 121 men in whom routine gastrointestinal x-rays were obtained at our request. Five of these ulcers were detected solely by routine examination; only three subjects had upper gastrointestinal and/or ulcer symptomatology at the time the diagnosis of ulcer was made. Two of these were actually hospitalized because of ulcer, the symptoms being so marked in one case that medical separation from the service was necessary. This was the only one of the 16 patients with ulcer who was unable to complete his obligatory period of military service. All eight cases were diagnosed within four months after the subject's induction, no further ulcer cases being detected in this group during the rest of the two years' service. The remaining ulcer cases came from the rest of our research population, and all of these men received x-rays because of the symptoms which brought them to seek medical care. These ulcers were detected 3 to 15 months after induction.

The source tables of the Medical Statistics of the United States Army, Annual Report of the Surgeon General, 1954, reveal an incidence of ulcer of 3.13 per 1,000 troops for the year 1954. Therefore, the total number of ulcers (16) discovered in our series (2,262 men) over a two-year period (3.54 per 1,000 per year) approximates the expected frequency of ulcer Army-wide.

Table 1.—*Distribution of Blood Types in Research Population**

	Total Population		With Ulcer		Without Ulcer	
Blood Group	No.	%	No.	%	No.	%
A	853	38.4	9	56.3	844	38.3
B	291	13.1	3	18.7	288	13.0
AB	83	3.7	1	6.2	82	3.7
O	997	44.8	3	18.7	994	45.0
Total	2,224	100.0	16	100.0	2,208	100.0

* p = 0.3 to 0.2.

Serum pepsinogen levels in the 14 subjects varied from 427 to 1,027 units with 10 falling within the hypersecretion category (fig. 1). The one subject with gastric ulcer had a pepsinogen level of 978 units, the second highest value among those with ulcer.

The mean of the pepsinogen values for the ulcer group is 707. With use of the *t*-test, the difference between the mean in subjects with peptic ulcer and the mean in the general sample (440) was found to be significant beyond the 0.001 level of confidence. Therefore, these findings are consistent with others that show that those persons who develop peptic ulcer come from that segment of the population with high serum pepsinogen values.[5]

ABO Blood Groups

Recently a great deal of work has been reported on the relationship of ABO blood groups with various diseases, especially those conditions associated with altered acidity of the stomach, e. g., gastric and duodenal ulcer, gastric carcinoma, and pernicious anemia. Aird and associates [3a] and Clarke and co-workers [3c] in England, Køster and co-workers [3b] in Denmark, and Buckwalter and associates [6] in the United States report that there is an increased frequency in the incidence of blood group O in patients with peptic ulcer as compared with controls and an increased incidence of blood group A (with a corresponding decrease in blood group O) in patients with such lesions as gastric carcinoma and pernicious anemia. In contrast, Clarke and co-workers [3d] present data, including sibship studies, indicating no such relationship.

Out of the total research population (2,262), 16 subjects developed ulcer (by x-ray diagnosis). In 2 of these 16, serum pepsinogen levels were not obtained and therefore were not included in the description in the preceding section. The blood type, however, was known for all 16. The distribution of blood types for our research population is shown in table 1. It will be seen that this distribution is approximately the same as that usually recorded for the United States. Of the 16 subjects with ulcers, 9 were group A, 3 group O, 3 group B, and 1 AB. This would seem to show that approximately 56% of the ulcer subjects were group A, whereas only 38% of the research population were group A and only about 19% of the ulcer subjects were group O as compared with 45% of the population. However, chi-square analysis of these data were not significant. (In all the chi-square statistical analyses in this paper, a p value of 0.05 or less was accepted as the level of statistical significance.) Consequently, in our series no relationship between blood type and the incidence of peptic ulcer was demonstrated.

As has been shown, attempts have been made to correlate ABO blood groups with peptic ulcer and pepsinogen with peptic ulcer. Mirsky [7] has analyzed data regarding the relationship between ABO blood groups and serum pepsinogen levels; no correlation was found. Køster and associates [3b] compared the blood groups of patients with conditions associated with low and high hydrochloric acid secretion in the stomach (fig. 2, *left*). They reported an increased frequency of blood group O and a decreased frequency of blood group A in conditions associated with increased acid production.

In our series, there were 2,014 subjects who had both pepsinogen levels and blood types available. When each pepsinogen secretion category is broken down into the percentages of ABO blood groups within it, and plotted on a graph, it will be seen that there is a trend not unlike that reported by Køster and associates, namely, with increasing pepisongen levels there is an increased frequency of blood group O and a corresponding decrease in blood group A (fig. 2, *right*). Blood groups B and AB show no such trend. However, plotting the blood

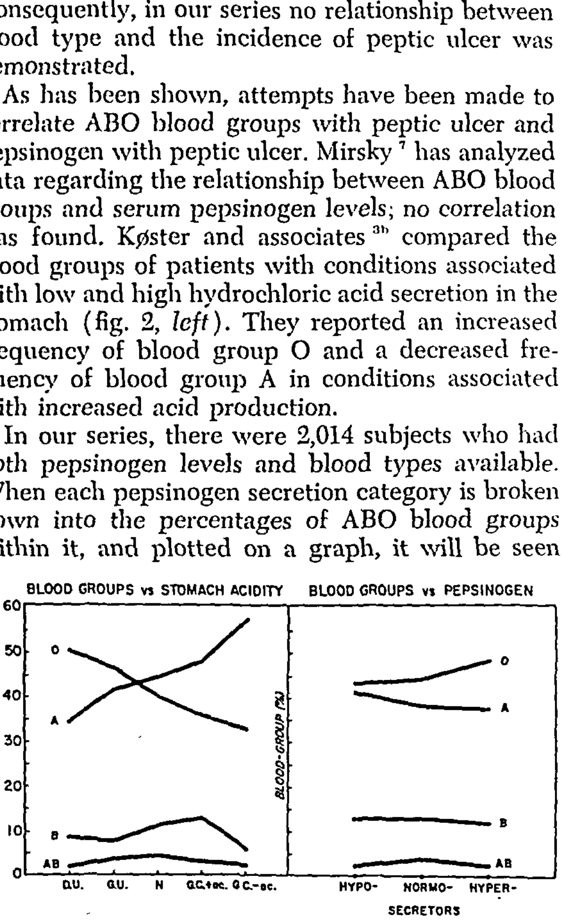

Fig. 2.—*Left*, frequency of ABO group in five different conditions of the stomach, ranging from hyperacidity to achlorhydria.[3b] (D. U. = duodenal ulcer, G. U. = gastric ulcer, N = normals, G. C. + ac. = gastric carcinoma without achlorhydria, G. C. — ac. = gastric carcinoma with achlorhydria.) *Right*, frequency of ABO groups compared with pepsinogen secretion categories in 2,014 Army inductees.

groups against secretor categories and analyzing these data by means of the chi-square test revealed no significant relationship. Consequently, the slight trend cited cannot be interpreted.

Pepsinogen and Behavior

The demonstrated relationship of high serum pepsinogen level and personality factors to the incidence of peptic ulcer, together with the evidence for the genetic determination of the level of serum pepsinogen,[5] raises the question of a possible relationship between serum pepsinogen level and personality factors. A relationship between "stress" and urinary excretion of uropepsin[8] further suggests a possible correlation of psychological and organic factors.

In the first publication from this project—analyzing the psychological data obtained on the "special group" of subjects with high and low pepsinogen secretion in our population sample—Weiner and co-workers[1] found a significant correlation between serum pepsinogen level and personality characteristics. The data used were the responses of the subjects to a battery of psychological tests, consisting of a group Rorschach, Blacky pictures, and Draw-a-Person test and, in addition, certain items of the Cornell Medical Index and Saslow test. They concluded that persons with hypersecretion showed intense "oral" needs, such as wishing to be fed, to lean on others, and to seek close bodily contact with others; if attempts to gratify these needs fail the resultant frustration causes anger which cannot be expressed for fear of a loss of the supply of these needs. They also felt that persons with hyposecretion had less problems of dependency but were more narcissistic, showing more problems relating to bodily discomfort and reacting to sources of discomfort with freely expressed hostility, some even showing hostile feminine identification which they defended themselves against by a masculine overcompensation.

TABLE 2.—*Relationship of Social Behavior and Background Factors to Pepsinogen Levels*

Behavior	p Value	Significant
Social (Performance)		
Final military performance rating	0.3-0.2	No
Court martial convictions	0.2-0.1	No
Court martial offenses	0.1-0.05	No
Number of times AWOL	0.5-0.3	No
Civil criminal record	0.7-0.5	No
Type of discharge	0.02-0.01	Yes
Medical		
Symptoms or complaints at induction		
CMI total "yes" responses	0.95-0.9	No
CMI stomach complaints only	0.5-0.3	No
Pathology, treatment, etc.		
Peptic ulcer	0.001	Yes
Treatment for other GI complaints	0.5-0.3	No
Outpatient medical record	0.5-0.3	No
Hospitalization		
History of any	0.7-0.5	No
Number	0.7-0.5	No
Days	0.1-0.05	No
Reason (GI or other)	0.2-0.1	No
Social Background		
Broken home	0.95-0.9	No
Age of broken home	0.10-0.05	No
Position in family	0.05-0.02	Yes
Social class affiliation	0.9-0.8	No

It is to be noted that the data used by Weiner and co-workers were directed toward defining personality characteristics but not toward describing overt behavior or predicting performance. Indeed, the results of the studies by Glass and associates[9] clearly indicate that a wide spread of personality characteristics is compatible with adequate to superior performance in a military situation. In order to investigate these questions further, possible correlations between the serum pepsinogen levels of our subjects were compared with data on military performance (1,999 subjects) and also with certain arbitrarily chosen items of social background (table 2).

Every individual was given an over-all performance rating for his military service by two officers conjointly (by one of us [P. G. Y.] and a psychiatric social work officer who had considerable past experience in commanding troops). The performance ratings given were (1) above average, (2) average, (3) below average, (4) failure, and (5) separately classified. (The details of this rating system, as well as the whole problem of performance and military effectiveness as it relates to numerous variables, is the subject of a separate study now in preparation based on this population sample.)

In order to be given an "above average" rating, a soldier had to have demonstrated clearly outstanding performance in a major duty assignment. A rating of failure was given when the subject failed to complete his obligatory period of military service because of such things as having received a medical discharge or discharge by a court martial or through administrative channels for unsatisfactory behavior. A fifth rating included such categories as hardship discharge and erroneous induction. This fifth rating was not included in the analysis, and the total number of subjects on whom the relationship of blood pepsinogen level to performance was based was, therefore, 1,999.

The average and below-average ratings were arbitrarily determined with the general principles utilized in the previous study on military effectiveness by Glass and associates.[9] In keeping with such studies, the performance of this sample showed that approximately 90% rendered satisfactory service (average and above-average ratings) and only about 3% were failures. From the performance standpoint then, this sample is a representative one. When these military performance ratings were compared with the pepsinogen categories and the data analyzed by means of the chi-square test, no significant relationship was found.

Table 2 shows the level of significance (p value) from the chi-square test of the relationship of the items of social behavior and social background which have been selected for comparison with serum pepsinogen levels. No significant relationship was found except for the type of discharge, presence of peptic ulcer, and position in family.

The relationship of the incidence of peptic ulcer, as already described, is highly significant. The item "type of discharge" refers to discharge from the Army for (1) completion of tour of duty, (2) medical reasons, and (3) administrative discharges, bad conduct discharges, or similar reasons. The low significance noted in the table was due to the fact that medical discharges (not for ulcer) were slightly higher in the hyposecretion group than would have been expected by chance distribution. Analyses of those discharges that reflect aberrant social behavior (i. e., administrative discharge) fail to show any relationship to pepsinogen level.

Except for peptic ulcer, items reflecting medical behavior (CMI, outpatient treatment, and hospitalization) failed to correlate with pepsinogen values. Whether a person was hospitalized or not, the number of hospitalizations, days of hospitalization, and the reason for hospitalization (i. e., for upper gastrointestinal complaints other than ulcer, compared with all other reasons combined) all fail to show any significant relationship to the serum pepsinogen values.

In the age group of this population it is clear that, other than peptic ulcer, the criteria for medical problems and the criteria for over-all military performance show practically no significant relationship with pepsinogen secretion categories. These results again emphasize the previously reported and generally accepted conclusion that subjects of widely varying personality characteristics or psychological make-up perform equally well in the over-all military requirements. The significant relationship of serum pepsinogen level to peptic ulcer is in striking contrast to all the other criteria examined.

Of the items of social background chosen, only the position in the family (oldest child, youngest child, only child, and other) shows a statistically significant relationship to serum pepsinogen level, the results of chi-square analyses of the data yielding p values of 0.05 to 0.02. An analysis of variance was performed on the frequency distribution of pepsinogen values in each of the four categories of position in the family. The F value resulting from this analysis was significant beyond the 0.05 level of confidence. Figure 3 shows the means for the position in family, and it will be seen that the rank order of these means (from highest to lowest) are oldest child, other child, youngest child, and only child. When *t*-tests were computed to compare the various pairs of means, it was found that the difference between the mean for the oldest child and the only child was significant at the 0.02 level and the difference between the oldest and youngest child was significant at the 0.05 level. The difference between oldest and other child was not significant.

The small absolute differences between the means of these groups and the possibility of a chance finding of a significant relation in any long series of tests of complex data suggest that this finding is not of practical importance and indeed may not be supported by further studies. One reason, however, for considering these data is that the rank order may be related to cultural attitudes not infrequently encountered in families of different size. Thus, the oldest child may experience a continuing state of responsibility combined with frustration in contrast with a state of "baby" of the family (youngest child) or of lack of competition for immediate "rewards" (only child). It may, therefore, be desirable in future studies to obtain childhood developmental data for comparison with serum pepsinogen levels. Such data would further clarify the problems of the reciprocal relationships between somatic and psychological factors and their propensity for modification by life experiences.

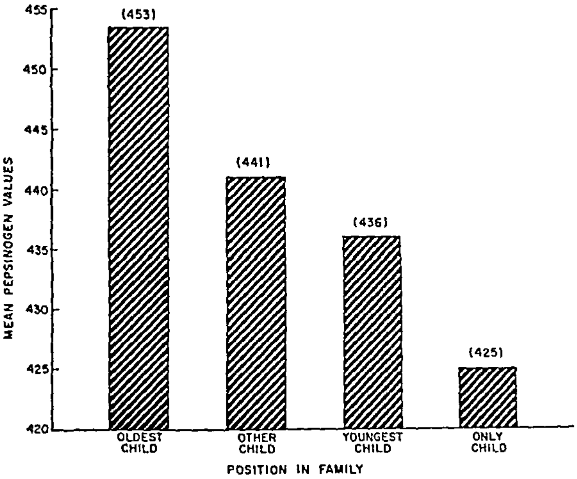

Fig. 3.—Rank order of distribution of mean pepsinogen values and position of child in family in 1,755 Army inductees.

Summary

The serum pepsinogen values found in 2,031 inductees ranged from 66 to 1,244 units. The mean was 440, and the standard deviation was 136. Hyposecretion was defined as a pepsinogen value less than one standard deviation below the mean and hypersecretion as pepsinogen values greater than one standard deviation above the mean.

Fourteen of these subjects developed peptic ulcer in the Army; 10 showed hypersecretion, 3 just below the cut-off point and only 1 as low as the mean of the total group. The mean pepsinogen value for the ulcer group was 707, and the difference between this and the mean of the total sample was significant beyond the 0.001 level of confidence.

No significant relationship between blood type and either peptic ulcer or serum pepsinogen was demonstrable. Pepsinogen levels failed to correlate with over-all military performance or other items chosen as objective measurements of social behavior. A slight positive relationship was found between position in the family and pepsinogen, the oldest child tending to have higher pepsinogen values than younger or only children.

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MSP H. A. Becker provided assistance in collection, coding, and analysis of these data. Statistical analyses were performed with the aid and supervision of Capt. H. A. Williams (MSC).

OUTWITTING ANTIBIOTIC RESISTANCE.—At Liverpool it has been customary in the past four years to treat male patients suffering from gonorrhoea with single injections of 0.5 g. of streptomycin. The numbers so treated were 215 in 1954, 231 in 1955, and 241 in 1956, and the results have been good. Nevertheless the proportion of failures increased from 2.3% in 1954 to 4.9% in 1955 and 7.0% in 1956. Alergant, who reported these facts, had not attempted to demonstrate streptomycin resistance in vitro, but had little doubt that streptomycin-resistant strains of the organism were emerging. Curtis and Wilkinson in London, found only 1 streptomycin-resistant strain of gonococci among 81 tested; and Cradock-Watson et al., also in London, found none resistant among 200 tested. The evidence suggests, therefore, that development of resistance is related to the local practice with penicillin-resistance in London where penicillin has been the drug of choice and streptomycin-resistance in Liverpool where streptomycin has been the routine remedy. Further data are required, especially on tests in vitro in Liverpool; but these findings may point the way to a means of dealing with this difficult problem. The evidence is scanty; but, such as it is, it suggests that sensitivity may perhaps be restored if the drug is withheld from patients with the infection. Dunlop showed that 86% of cases of acute gonorrhoea seen at the London Lock Hospital in 1946-47 were resistant to treatment with sulphonamides; but Cradock-Watson et al., who tested their 200 strains of gonococcus for sensivity to sulphathiazole, found to their surprise that 199 of them were inhibited by 8 mg. or less sulphathiazole per 100 ml. A concerted policy of changing from one remedy to another in selected areas, at agreed intervals, might help to preserve the efficacy of these drugs; but much more information is required before such a plan can be advocated with confidence.—Annotations, The Treatment of Gonorrhoea, *The Lancet,* October, 1958.

THE SINGLE SEIZURE–ITS STUDY AND MANAGEMENT

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It is impossible to tell whether a single convulsive seizure occurring in a given patient is destined to be his only seizure or whether it will prove to have been the first of a series. A study is made of 48 single or first seizures in patients who ranged in age from 2 to 66 years in an effort to identify factors that might have prognostic value. Of the 48, 13 had subsequent attacks. Thus, a single seizure should not be taken lightly, and an aggressive program of neurological and electroencephalographic diagnosis is called for. In some instances the diagnosis clearly calls for medical or surgical treatment, but in general the 27% likelihood that there will be at least one more seizure justifies anticonvulsant medication. If the patient is kept free from seizures for two years, it may be safe to carry out a gradual termination of the medication.

The single seizure presents a problem as old as any in the field of epilepsy. There are many persons who have had a single seizure and never had a recurrence. Each of the million or more patients with known recurrent seizures must have had such an initial attack, and the physician, at that time, had no way of knowing what the future course would be. With increasing public education and wider recognition of epilepsy, we will have increased opportunities to see persons after these initial attacks.

However, if one consults the average medical library for guidance, one is surprised to find relatively little help available on this point. Almost all textbooks of medicine, neurology, or pediatrics define epilepsy as a "recurrent illness" and remain silent on what to do while waiting for it to become recurrent. A few more recent references consider the problem briefly and often with divergent conclusions. Because of these uncertainties, I will review these points of view and outline some preliminary observations in a longer range follow-up study of patients first seen after a single seizure episode.

Occurrence of Single Seizures

The term seizure, or epileptic seizure, encompasses a variety of patterns signaling different things to the observer. From the practical point of view, most patients with single seizure problems will have a grand mal attack or more protracted focal motor or psychomotor attack. Cases of petit mal, subjective sensory, or brief psychomotor attacks will seldom be witnessed by an observer astute enough to bring the patient to a doctor's attention.

As is true throughout medicine, we cannot forecast the future for an individual person, but we can learn about it and be guided to probable patterns by experience with others with the same or related problems. For example, Lennox has observed an incidence of seizures in 5% of all children under 5 years of age, one-half of these being related to febrile illnesses. Livingston found that 5% of patients with this type of febrile convulsion later had chronic seizures, this being more likely if there were focal aspects, a long seizure, positive family history, or an abnormal electroencephalogram (EEG). Alpers found patients with only one to three seizures in an entire lifetime to have electroencephalographic evidence of abnormalities and to be susceptible to alcohol, stress, or fatigue. Even after seizures have become recurrent, "cures" without medication are cited by Penfield and Erickson as occurring in 5 to 13% of cases. Wilkins found remissions in 41% of patients with infrequent seizures, and Lennox observed spontaneous remissions for one to five years in 23% and for over five years in 6% of his epileptic patients. These data are mentioned to indicate the variability of outlook for patients with single, as well as multiple, seizures.

Methods and Results of Study

The Latter-Day Saints Hospital EEG Laboratory was opened in January, 1950, to serve a representative cross section of patients having a variety of neurological disorders, with a 2:1 proportion of outpatients to inpatients. For present purposes, records for the five-year period up to Jan. 1, 1955, have been reviewed. The original doctors' records have been checked as to follow-up status for three and one-half to eight and one-half years and letters sent out to patients to check on the remainder. In the five years, 48 of a total of 1,054 electroencephalograms were studied because the patient concerned had had only a single seizure. A breakdown of these cases may clarify the nature of the problem and help in planning further study and treatment.

The patients referred for electroencephalographic study after a single seizure ranged in age from 2 to 66 years, but two-thirds of them were about

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From the Dr. W. H. Groves Latter-Day Saints Hospital.

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equally distributed through the 30-year span from 21 to 50. It is felt that this pattern may simply reflect a greater medical nonchalance toward seizures early and late in life.

Electroencephalograms were found to show generalized abnormality in one-half, localized abnormality in one-fourth, and normal findings in one-fourth. All seizures were reported as generalized except one that was in the right arm only and one that began with unilateral jerking. A family history of seizures was present in only 12.5%.

The underlying pathological basis for the seizure was not clearly defined in over half the cases, although many of the patients had x-rays, spinal punctures, air studies, or other examinations. The remainder appeared related to trauma, encephalitis, alcohol, insulin, cerebral Hodgkin's disease, or carbon monoxide exposure. The patients with encephalitis and Hodgkin's disease died, and the disease was confirmed by autopsy. No primary brain tumors were found in this series. Of the 48 patients seen after a single seizure, 13 (27.3%) had subsequent attacks, which occurred from a few days to a few years after the patients first were seen. All of these recurrent attacks were generalized, although only half of the electroencephalograms showed generalized abnormality. Only 1 of the 13 patients had had a normal electroencephalogram, and one had a family history of seizures. Age range and distribution of the apparent causes was similar to those of the larger group. Except in the patients with fatal cases of encephalitis and Hodgkin's disease, findings on x-rays and spinal fluid or air studies were negative. Seizures were well controlled subsequently with diphenylhydantoin (Dilantin) sodium therapy when it was used consistently. In some cases, medication was later gradually decreased without further recurrence of seizures.

Management of the Patient

With this background, we can turn to the problems involved in study and management of the patient who has had a single seizure. All too frequently, this consists of a brief, incomplete, often telephoned report of the attack, followed by a general reassurance by the physician that it will not happen again.

It is of primary importance to establish from the beginning, as definitely as possible, that one is actually dealing with a seizure problem, since some harm may result from the overzealous study and treatment of hysterical or other episodes resembling seizures. The electroencephalogram is helpful, but it cannot be used alone for differentiation. Nothing can substitute for an accurate, detailed history, with an insistence at all times on an objective, eye-witness description if anyone saw any part of the attack. Particular attention is paid to contributory factors, as, for example, in alcoholism, where a somewhat different situation prevails in which primary attention to the alcohol problem may be more important.

Similarly, these cases underline the importance of additional first-level studies, including a review of the general medical history, the general physical and neurological examination, routine blood and urine studies, and any special studies suggested by these.

As for a second level of studies, such as x-ray and electroencephalogram, Doyle and others have suggested delaying until a second seizure, specifically in febrile convulsions, while Crawley, Forster, and Chao and others are less definite but imply that an examination, including x-ray and electrocardiogram, are ordinarily done after a single seizure.

Another level of studies, such as spinal fluid examination, air studies, or angiograms, should follow if specific indications appear in the course of the first two levels of study, but the latter are used less routinely where there is greater interest in the electroencephalographic evaluation. Our material is too limited in scope as yet to do more than suggest concurrence with these principles.

Even a single seizure should not be taken lightly; thus, if the first physician consulted does not feel equipped to evaluate the problem, he should enlist the assistance of someone who does have the time and interest to do so.

This careful evaluation of the patient sets the stage for appropriate subsequent management. Wherever specific pathology is disclosed, specific measures are taken, whether these are neurosurgical or they lie in treatment of concurrent medical illness. In addition, common sense advice about regularity of meals, work, and sleep or limitation of the use of alcohol or stimulants is appropriate, as with other patients with seizures, including any special considerations involved by the patient's social or occupational setting.

Medication

Next is the thorny problem of medication. In the past, most writers have waited for recurrences. More recently, Crawley and Chao have suggested treatment in selective cases but delay if the neurological and electroencephalographic findings are negative in either adults or febrile children with convulsions. In the latter group, Schmidt emphasizes the real potential hazards of seizures and urges anticonvulsive drugs in all cases, at least until the patient is 3½ or 4 years of age. The suggestions that neurological or electroencephalographic abnormality makes seizure enough more likely to warrant treatment appears sound. Farmer takes a yes-no position considering the severity of the attack, the patient's occupation, and other factors.

My experience in seeing over 27% of patients with a single seizure who have subsequent seizures suggests a somewhat more aggressive approach.

It is proposed that, after an initial major seizure, medication be suggested to the patient as the safest program for him if (1) he can and will intelligently adhere to a regular schedule and (2) he will report for periodic follow-up neurological examination and less frequent follow-up electroencephalographic study.

Outside of a hospital, there is a great difference between ordering a medicament and being sure it is taken. As in diabetes and similar conditions, education of the patient is essential to cooperation, and this is best done by the physician. Use of medication facilitates follow-up study, but the initial planning discussion is the best opportunity for reaching a mutually acceptable plan.

Some patients deny their illness or are set against any kind of medication and will stop it at the first excuse. Others are so apprehensive about their jobs or social status that they overlook advantages of medication. A frank discussion of the pros and cons of medication may include some of the ideas in the table.

Advisability of Medication After a Single Seizure

Problem	Pro	Con
Recurrence	28% in present series	Uncertainty
Medicament	Relative safety	Cost; bother; risk of interruption
"Masking" of disease	No effect on neurological or major electroencephalographic changes	Confusing if original diagnosis is doubtful
Threat of job loss	Minimized by prevention	Increased by disclosure of taking medication
Social stigma	Minimized by prevention	Established by use of medication

The risk of interruption of medication precipitating seizures can be minimized by the patient's cooperation. The risk of masking seizures by medication has been overemphasized and is minimized by careful follow-up study. In the job and social area, medication can be a two-edged sword, being protective in preventing seizures, but, potentially, putting the patient in a lesser jeopardy by permitting his need for such medication to become known. The latter can be minimized by simplification of dosage schedules to avoid his taking the medicament at school or work.

Once a medication schedule is set up, the interval management depends entirely on the patient's response and on follow-up examinations as a basis for future planning.

In the absence of other specific criteria, gradual termination of medication should be done in a fashion similar to that used with recurrent seizures. Most authorities suggest about a two-year period of freedom from seizures before this is done, with variation according to the electroencephalographic and other findings in the individual case. Should a seizure recur, medication is resumed.

Summary

The single or initial generalized seizure is a relatively frequent problem, appearing as the reason for 1 of 22 routine electroencephalographic studies at the laboratory of the Latter-Day Saints Hospital. Over 27% of the patients are known to have had subsequent seizures within a few days or a few years afterward.

Because of the relatively high risk, after careful neurological and electroencephalographic study an anticonvulsive medication program should be proposed to the patient and a mutually acceptable plan of management worked out with him to prevent some of the serious handicaps accompanying recurring seizures.

CLINICAL NOTES

REMOTE CONTROL TYPEWRITER FOR PARAPLEGICS

Alan Ziskind, M.D.
and
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A control panel has been designed to enable an individual who has lost the use of his extremities to operate a typewriter at a speed and accuracy comparable to that of the average nonprofessional typist. This apparatus was developed after observing patients with neuromuscular disabilities attempting to strike the ordinary typewriter keyboard with the usual available devices. It was felt that, if a device could be constructed to allow such patients to typewrite with accuracy at a normal speed, their rehabilitational goals could be more readily and rapidly achieved. Not infrequently, the written word is the chief method of communication for these patients.

Working on the principle that neck and head muscles have the greatest residual muscular control in many instances, a remote control typewriter

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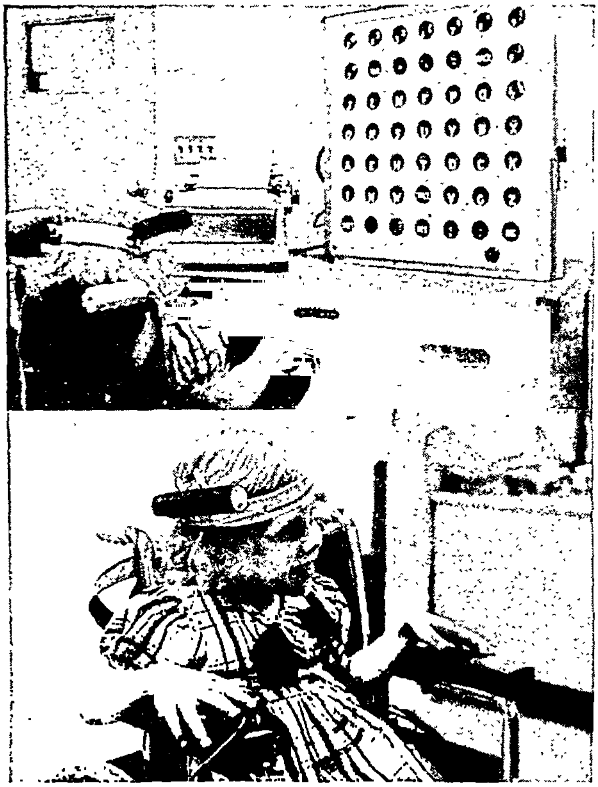
From the departments of pediatrics, Boston City Hospital and the Boston University School of Medicine.

was designed to enable the patient to type with the use of this group of muscles. The photoelectric cell panel board contains a specific target area representing each key of the typewriter. This is coupled to a standard electric typewriter through an easily attached solenoid box placed over the typewriter keyboard (see figure). When a parallel-beam light source from a small head lamp strikes the desired target area, the letter is automatically printed. Thus, depending on the distance between light source and target board, a very small change in head position causes a relatively great excursion of the light beam on the panel. For practical purposes, a 15-degree motion of the head from a central plane in any direction is sufficient to actuate any area of the panel board.



Top, photoelectric cell panel board connected to standard electric typewriter with solenoid box over keyboard. *Bottom*, small head lamp with parallel beam to strike letter on panel board.

The light beam is sufficiently small so that it cannot focus on two target areas simultaneously. Because of the problem of unintentionally sweeping over many letters in the process of selecting the desired one, a small microswitch is interposed in the circuit between the panel board and the typewriter. While learning to operate the typewriter, the individual must close this switch to complete the circuit and print a letter. Since only a small movement is necessary to operate the switch, it is easily controlled by an elbow, finger, or any area of the body where minimal motor function persists. When greater proficiency is developed, the switch is used less often since the alphabetic distribution on the board is arranged so that letter sequences form common combinations and words, and modifications are easily made for the most effective operation.

The apparatus is best suited to patients who have lost the use of their extremities through injury or spinal cord disease. There is limited applicability to the cerebral palsied or athetoid patient. Individuals with residua from poliomyelitis and those with spinal cord injuries are able to type at a rate approaching 30 words a minute. A companion device—a battery-powered court stenographic machine—is being modified to allow an individual to attend school and take lecture notes which later can be transcribed at home.

It is hoped that this device will give many of the disabled more freedom of communication, which in turn will result in improved rehabilitation and emotional adjustment.

818 Harrison Ave. (18) (Dr. Alan Ziskind).

This study was aided by a grant from the United Cerebral Palsy Foundation.

ICTERUS NEONATORUM WITHOUT ISOIMMUNIZATION.—That the premature infant can develop kernicterus in the presence of hyperbilirubinemia without evidence of isoimmunization is becoming more generally accepted. . . . The bulk of the evidence indicates that premature infants exhibit jaundice and hyperbilirubinemia more frequently and to a greater degree than is reported in full-term infants. The duration of this hyperbilirubinemia is related to fetal maturity, persisting longer in the most immature infants. Because of the variability of concentrations of bilirubin in the plasma of premature infants, and because of the multitude of factors that play a possible role in determining the ultimate concentration of bilirubin, routine exchange transfusion for elevated concentrations of bilirubin does not seem warranted. The critical level over which exchange transfusion should be done cannot be stated on the basis of any available data.—G. H. Holman, M.D., Studies on Physiologic Hyperbilirubinemia of Negro and White Premature Infants, *Pediatrics*, December, 1958.

COUNCIL ON DRUGS

Report to the Council

The Council has authorized publication of the following report.
H. D. Kautz, M.D., *Secretary.*

The following report has been adopted by the Committee on Research.
Norman De Nosaquo, M.D., *Secretary,*
Committee on Research.

EXPERIMENTATION IN MAN

Henry K. Beecher, M.D., Boston

Present Aims

Experimentation in man for scientific purposes is as old as recorded history. The need for constant examination of the procedure is equally ancient. This is required by progress in science and by the advance of ethical and moral concepts.

In the two decades just passed, two reasons have emerged which especially point up the need for a new review of the subject. First, there were the outrages of Hitler's Germany. The puzzle is how such things could have occurred in modern society. Although the philosophical problems raised by those gross actions are beyond the area surveyed in this report, they too indicate the need for a long, straight look at our current practices. Second, there is the rather newly recognized fact that some types of basic scientific advance can be made only in the presence of disease. Nature presents us with bolder experiments than we would ever dare to perform ourselves. We profit from a study of them—basic science profits. Having seen what fundamental ends can be achieved, the experimentalist is led to carry on where Nature leaves off. The purposes of human experimentation thus become deeper and more complex than ever before, and so also do the problems surrounding it, reasons enough for this study.

In most cases, the problems of human experimentation do not lend themselves to a series of rigid rules. Although one purpose of the present study is to set down views, concepts, and even "rules" that have been accepted by one group or another, this is done so that the investigator, troubled by a given problem, can find references to past thinking on this subject, and so that he can have a framework against which he can measure his problems in terms of the experiences and conclusions of others in similar situations. The breaches of ethical conduct which have come to my attention were owing to ignorance or thoughtlessness. They were not willful or unscrupulous in origin. It is hoped that the material included here will help investigators protect themselves from the errors of inexperience.

Finally, it can be said that, while human experimentation has accompanied the practice of medicine from times of antiquity, the current concept of medical research has not really been presented as such to the courts. As the courts have understood it, human experimentation has not been, nor is it now, legally recognized as a legitimate part of the physician's activities. "So far, planned and directed medical research on human beings has not been tested." [1] The universal and long-standing recognition that research is essential to the advancement of medical science and the newer recognition that some aspects of basic science cannot advance without it have led to a correct, although still extralegal, expansion of human experimentation. Curiously, such work, when well conceived and soundly conducted, is everywhere recognized as being properly within the ethical and moral concepts of our time; yet it remains outside legally. Legal inclusion will depend on an understanding of all the facets of the problem.

Brief History

The oldest world literatures contain references to experimental work with animals and man.[2] It was the practice in ancient Persia for the king to hand over condemned criminals for experimental purposes in science. Later the Ptolemies did the same in Egypt.[3] About 1,800 years ago Galen, the founder of

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From the Anesthesia Laboratory, Harvard Medical School at the Massachusetts General Hospital.

experimental physiology,[4] somewhat formalized medical experimentation, but this fell under a cloud during the Dark and Middle Ages, until Vesalius in the 16th century overrode the proscription against dissection of the human body and demonstrated certain errors in Galen's concept of the circulation of the blood. Three generations later Harvey, after carrying out controlled experiments in animals and in man,[2] demonstrated the circulation of the blood. He showed, in particular, that all the blood had to pass through the heart (if his calculations of volume and velocity were correct), and thus the first idea of measurement in biological investigation bore fruit.[4] More than 100 years later, Lind, in 1747, carried out a remarkably well-controlled study and demonstrated that oranges and lemons could cure scurvy. A half-century after this, in 1798, Jenner, after controlled experiments in man, published his proof of the value of vaccination against smallpox. The world was ready for two of its greatest experimentalists, Claude Bernard and Louis Pasteur.

However, all was not smooth sailing for the eager investigator. Experimentation on other men requires a willingness to experiment upon oneself as evidence of good faith, although in a given case self-experimentation may be wholly impractical. When it is carried out, it must be done with the same safeguards that are applied to other subjects. Ivy[2] cites a number of examples to indicate that willingness without the discipline of proper controls can be misleading or devastating, or both, to the participant. In 1767, John Hunter inoculated himself with gonorrheal pus to prove that the disease was transmissible in this way. He succeeded. But from the same inoculum he also acquired syphilis and concluded that gonorrhea and syphilis were merely manifestations of the same disease. Purkinje gave himself enough digitalis to kill nine cats, so that he might study the visual changes in himself. He had cardiac pain and irregularity and vomited for a week. Hales, enthusiastic about the marvels of intravenous injection, received a half-ounce of castor oil by this route and lived to describe its remarkable effects. In 1830, Tonery, in order to convince the French Academy of the extraordinary powers of charcoal to absorb alkaloids, took with this safeguard a dose of strychnine which, without it, would have been lethal. In 1857, carbon tetrachloride was tried as an anesthetic in man; a few animal experiments would have shown it to be unsuitable. In 1894, Oliver told Schafer that he had made extracts of all the endocrine glands and had injected them into his own son. Schafer altered the experiment and was first to demonstrate the pressor effect of epinephrine in dogs and cats. Ivy concludes that "these experiments may be a tribute to the enthusiasm and bravery of these early medical scientists, but they clearly show the limitations and dangers of uncontrolled self-experimentation."

At the present time we find that able men are still in difficulties. When one shifts from a study of objective manifestation of disease to subjective effects, specifically, for example, to a quantitative study of the effects of drugs on symptoms, it becomes apparent that added controls are mandatory. Chief among these is the use of the double-unknowns approach to eliminate bias. This procedure is not possible when the experimenters are also the subjects, who, as drug experience and sophistication grows, cannot remain in ignorance of the "aura" produced by opiates, for example. The scores of studies that have been lost because of a failure to recognize and employ adequate controls have been reviewed elsewhere.[5]

Paradoxically enough, in the last century at least, those who experiment in man have been freer of attack than those who carry out animal experimentation. The ethics of human experimentation will be discussed later.

Scope

There are many good reasons for a careful consideration of the scope of human experimentation: protection of the subjects, the goals of the investigators, their research and their institutions, and the sound development of medicine. These all require a levelheaded approach to experimentation in man.

Comparatively recent developments in medicine and changes in emphasis give added weight to an examination of human experimentation at this time. Although prior experimentation in animals is absolutely necessary when possible, the crucial study of new techniques and agents must be carried out in man. The extraordinary skill of the organic chemist and the biologist, working together in identifying active agents in natural products, and the chemist's progress in creating new and promising compounds, which ultimately must be tried out in man, throw an exceptionally heavy load on the experimentalist. Man as the final test site has come into prominence only in recent decades. The current development of human biochemistry, human physiology, and human pharmacology has made it plain that man is the "animal of necessity" here. In addition, there is a new interest on the part of the truly basic scientist in human experimentation. This will be described in terms of the scientist's goals.

The investigator has many goals, and, in many aspects, they are like those of the practitioner in ultimate aim. The investigator is concerned with health and its preservation and the betterment of life as well as with the causes and consequences of disease, the mechanism and relief of its symptoms, correction of its signs, prevention of lasting effects of disease, and the very eradication of disease. Activities directed toward these ends involve, very often, alteration of function of the body or the mind, in health or in disease, "directly or indirectly, in individuals or groups, primarily for the advancement of . . . human welfare. Although use of a procedure or its withholding may directly benefit the person involved, its basic purpose is for elucidation and generalization."[6] When possible, investigation begins in animals but finally must be applied to man.

The goals mentioned are ancient ones. There is a new one or, more accurately, a newly recognized one. In the last decade or so, it has become increasingly clear that the study of disease in man can have a deeper meaning than once was believed to be the case. The view was widely held (and still is in some quarters) that the study of disease at the bedside level represents nothing more than applied science at best. A more thoughtful approach could long ago have led to a broader grasp of the situation: some parts of basic scientific advance (I use the term in its classical sense) are utterly dependent on disease. An abundance of examples comes to mind. Pauling's interest in "molecular disease" arose in part from work with abnormal forms of hemoglobin. Although neurophysiologists have long been interested in the biochemistry of the potassium ion, recent basic advances in knowledge of this ion have come from studies of dehydration. Knowledge of the physiology of the endocrine glands is largely indebted to the fundamental leads found in disease. The anatomy of the central nervous system has been learned, in significant part, by study of cerebrovascular accidents. Such diverse matters as the discovery and understanding of vitamins, the development of microbiology, and even the advance of genetics in study of hereditary factors in disease leave no room for doubt that truly basic science can be advanced by a study of disease processes. This awareness leads to a further extension of human experimentation. With these developments it is time to examine the many-faceted problem of experimentation in man.

Ladimer[6] has expressed it thus:

> Properly conducted experimentation [in man] by qualified scientists must therefore be considered an integral branch of biologic and medical science, but it does not thereby become customary medical practice. Nor does its essentiality and acceptance establish clearly its character or place the methods employed beyond scrutiny. The responsible professions have a duty to delineate for their own members and for a critically vigilant public the nature of medical research and the limits within which it may be properly undertaken.

These introductory remarks can be concluded with the comment that prevention of experimentation can also be an experiment, even a very dangerous one, as, for example, withholding treatment of a control group. If experimentation is to be withheld, "it should be demonstrated that the proposed experiment is more dangerous or more painful than the known [or probable] results of inaction."[7] This is an expression of an ideal, rather than a practical, possibility in most cases.

Throughout this article the aim has been to present sound background data, common-sense views, and principles of procedure rather than rules. The intricate considerations which must be brought to bear on this general subject leave room for only a few absolute statements. These are discussed in the section on Codes.

Social Necessity

In the foregoing remarks it is clearly evident that human experimentation is essential for the welfare of the race, for in medical research lies "a common benefit not obtainable by other means."[6] The development of medicine, the safeguarding of health, and some types of basic scientific advance all require human experimentation. With the recent Hitlerian acts freshly in mind, it is not surprising that responsible investigators are wary of such phrases as "for the good of society." In any case, the scientist or physician has no right "to choose martyrs for society," as Kety[8] has put it.

> It should be apparent that no stigma is attached to the performance of human experiments *per se*; disgrace and infamy can arise only through its misuse. The moral obligation of performing all human experiments, with due regard to the sensibility, welfare, and safety of the subject, must not be violated. As phrased by Claude Bernard in 1856, "Christian morals forbid only one thing, doing ill to one's neighbor." So, among experiments that may be tried on man, those that can only do harm are forbidden, those that are harmless are permissible, and those that may do good are obligatory.[9]

Unfortunately, decision is usually not so simple as this sounds; choice often lies among various shades of gray, not between black and white. The social necessity for experimentation in man operates, of course, only when the desired ends cannot be obtained in other ways, as through experimentation in animals.

Subject

Observations on the choice of a subject can be set down as follows:

1. It is often not possible to directly transfer observations made in normal individuals to the sick. The complexities here are so great that only one or two suggestive examples can be mentioned: (*a*) It is exceptionally difficult, if not impossible, to reproduce usefully in normal subjects symptoms which ordinarily arise in disease. Take, as an example, pain. Beecher[5] has compiled evidence which supports this view, in that 15 groups of investigators attempted but failed to show a dependable

relationship in man between pain threshold and the action of analgesic agents, notwithstanding scores of papers to the contrary. (*b*) There is no assurance that the high incidence of nausea in normal individuals after administration of morphine holds true for those who are in pain. Incidentally, this points to a problem not yet satisfactorily solved, that is, how to secure information on the side-effects of therapeutic agents when these side-effects may be similar to those present at times in the disease state studied.

2. Individuals who may die suddenly or who seem to be in imminent danger of death should not, under ordinary circumstances, be chosen as subjects for experimentation, however harmless the planned procedure may be. If death occurs during such an experiment, it could cast a shadow over a potentially valuable agent or useful technique, not to mention placing the investigator in a most unhappy predicament, where, although innocent, he may appear guilty.

3. It is usually unwise to study a therapeutic procedure in an individual who has also a disease unrelated to the expected therapeutic effects.

4. Lay subjects, sick or well, are not likely to understand the full implications of complicated procedures even after careful explanation.

> To obtain the consent of the patient to a proposed investigation is not in itself enough. Owing to the special relationship of trust which exists between a patient and his doctor, most patients will consent to any proposal that is made. Further, the considerations involved are nearly always so technical as to prevent their being adequately understood by one who is not himself an expert. It must, therefore, be frankly recognized that, for practical purposes, an inescapable responsibility for determining what investigations are, or are not, undertaken on a particular patient will rest with the doctor concerned. Nearly always his judgment will be accepted by the patient as decisive.[10]

Or, as Guttentag[11] has put it, "one has only to think of present-day specialization in medicine in order to realize that the patient is frequently not able to grasp all the implications of a certain procedure so far as his health is concerned."

To some, this complexity leads to a strong admonition concerning voluntary work. At one time, Pfeiffer[12] held the view that one should "never use anyone except a volunteer who is at least at the level of a graduate student and who has investigated for himself the nature and possible dangers of the drug or procedure involved." Many investigators would not agree with this last view. For some types of investigation, especially when subjective factors are involved, it is essential to have subjects who know nothing about the expected results and have no vested interest in the outcome. Certainly Pfeiffer's early requirement for an informed subject cannot be complied with in the case of the diseased subject. Such difficulties, however, emphasize the increased responsibility of the investigator when the subject cannot truly understand the full implication of the study contemplated. This view is set down in some detail for comparison with this idealistic, yet thoughtful and practical, investigator's current view. Pfeiffer[13] states his present view: "My quotation from 1951 must certainly be modified as of this date since we are using prisoners at the Atlanta Penitentiary who are not graduate students! We do screen our prisoners for psychiatric difficulties by having them complete a Rorschach examination, IQ assay, and MMPI tests. We also go over their psychiatric history very carefully. My statement of 1951 represents the ideal situation rather than the practical situation."

Volunteer

Information Given.—The information given to or obtained by the volunteer subject may vary widely from none at all, when innocuous procedures are undertaken in the study of subjective responses, to full discussion whenever any risk is involved. These matters have been referred to in the preceding section.

Laboratory Personnel and Medical Students.—Laboratory personnel and medical students are often considered legitimate game by the eager but impoverished investigator, and certainly tradition has accepted their use. In my opinion, at least, there are two reasons why such groups are usually not a good choice: 1. In a sense, these are captive groups, not so seriously so as prisoners of war perhaps, but nonetheless available for certain kinds of subtle coercion. A volunteer should be just that, not one who may be subject to fear of the consequences if he does not cooperate. The more domineering the investigator, and thus the more valid the point made, the more likely is this possibility to be disclaimed. Denied or not, the situation does exist; it is better to avoid it. 2. In quantitative studies of subjective responses over many years, it has become clear to me that, in this field at least, subjects must not be in communication with each other, for, if they are, certain false "syndromes" are "established," through conditioning presumably. Lack of space precludes citing some startling examples of this. The hazard to sound conclusion of such action is nowhere more amusingly evident than in the reports of some of those who have studied the effects of psychotomimetic drugs in their own personnel.

Mackintosh,[14] however, has expressed a sound and considerate point of view concerning the use of laboratory personnel:

> On the difficult question of laboratory personnel, we had certain decisions to make in the London School of Hygiene. In the study of malarial parasites "resting" in the human liver we had offers from a skilled technician to submit himself to infection and then to have a small liver section taken. In this case the technician was a senior man who was fully aware of the risks involved. His offer was gratefully accepted, but at the same time a regulation was passed that in the

> future no human experiment should be allowed without a full report being made in advance to the School Council (which is the professional body) and to the Board of Management, which has a considerable representation of scientists, and also lay members. The crux of the decision was whether the volunteer had the training and skill to appreciate the whole situation, although not necessarily the details of the procedure. It was evident that there might be subjective matters of study which the volunteer ought not to know beforehand, so as to avoid vitiating the experiment. The additional point of the decision was to make sure that the volunteer gave his consent freely, or, better still, offered his service in writing. In such cases no fee or reward, apart from any out-of-pocket expenses, should be offered.

Lasagna and von Felsinger[15] have discussed the "ample reason(s) for wariness in making generalizations regarding drug effects from a study, no matter how careful, of any *single* group of individuals, be they sick or healthy, volunteer or non-volunteer."

Civil Prisoners.—The major scientific contributions which have come directly from utilization of civil prisoners who have volunteered for such endeavors offer at least a pragmatic justification for the practice. Possibilities for direct or indirect coercion, flagrant or subtle, are so great that use of these individuals must be considerate indeed to be sure that there has been no coercion. The practice has a rather long history. Included as civil "prisoners" are the inmates of orphanages[16] and asylums for the insane[17] as well as prisoners in jail.[18] During World War II both federal and state prisoners made important contributions to malaria studies, the use of blood plasma, plasma fractions, and plasma substitutes, and trials of various new drugs. In most prisons more volunteers were available than were needed.[2]

The advisory committee[18a] appointed by Governor Green, of Illinois, had this to say:

> Since one of the purposes of the parole system is reformative, the reformative value of serving as a subject in a medical experiment should be considered. Serving as a subject in a medical experiment is obviously an act of good conduct, is frequently unpleasant and occasionally hazardous and demonstrates a type of social consciousness of high order when performed primarily as a service to society. The extent to which the service of a prisoner in an experiment is motivated by good social consciousness on the one hand and by the desire for a reduction of sentence in prison on the other is a matter for consideration in the case of each prisoner. Regardless of a prisoner's motives for volunteering for an experiment, a habitual criminal or a prisoner who has committed a notorious or heinous crime should not be considered an acceptable volunteer for a medical experiment.

The rewards for prisoner volunteer service vary all the way from gifts of tobacco[18c] to a full pardon.[18b] Cautioning against excessive rewards, the Green committee said:

> The most important requirement for the ethical use of human beings as subjects in medical experiments is that they be volunteers. Volunteering exists when a person is able to say "yes" or "no" without fear of being punished or of being deprived of privileges due him in the ordinary course of events.
>
> A reduction of sentence in prison, if excessive or drastic, can amount to undue influence. If the sole motive of the prisoner is to contribute to human welfare, any reduction in sentence would be a reward. If the sole motive of the prisoner is to obtain a reduction in sentence, an excessive reduction of sentence which would exercise undue influence in obtaining the consent of prisoners to serve as subjects would be inconsistent with the principle of voluntary participation.

The committee added the somewhat unrealistic comment: "Obviously no one may make representations to a prisoner concerning the extent and types of reward which may accrue as a result of his service as a subject in a medical experiment." In all examples I have seen, the terms were explicitly stated beforehand and were always lived up to after the fact.

Military Prisoners.—It is never permissible to use prisoners of war for experimentation. This is the sound policy of the Department of Defense.

Volunteer Corps

Hogben and Sim[19] have this to say:

> If we approach the problem [of human experimentation] against a background in which the major advances of medicine occurred in the social setting of pestilences, practical difficulties of enlisting volunteers without violence to ethical standards are easy to exaggerate; but a wholesome regard for the sanctity of life becomes increasingly less relevant to a statement of the priorities of medicine in western communities with a life-expectation well above 60 years at birth. There is indeed an ever more pressing need for knowledge about many once-thought *minor* evils. We cannot effectively tackle them by group methods; but we might well do so with the help of individuals now willing to risk life or limb on the speedway or in the ascent of Mount Everest, if we could institutionalize a not uncommon appetite for adventure consistent with acceptable moral standards. It is not beyond the reach of social engineering to create a new corps of civil defence with that end in view. The voluntary response to the appeal for blood donors disposes of doubts about the feasibility of such an undertaking, if sponsored by an adequately accredited organization.

We have in the United States the beginnings of such a corps in the group of conscientious objectors to military service who volunteer, and also in the Mennonite group of young adults who volunteer as subjects for scientific studies.

Investigator

Characteristics and Qualifications.—The physician and the investigator are different in their procedures, in their aims, and in their immediate ends. To paraphrase Ladimer,[6] the physician accepts patients and is mainly concerned with their welfare; the investigator selects subjects (problems as well as individuals) and, while responsive to the patient's interest, is bent on solving the scientific problem. But "one irresponsible investigator can do great harm to medical science."[20]

All the so-called codes as guides to human experimentation emphasize the necessity that the experimenter be well trained and adequate as a scientist

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This relationship very often is identical with the patient-physician relationship and will be considered from that viewpoint. There is good reason why this facet of the human experimentation problem should be considered. Whenever the physician tries out a new drug or a new technique—not necessarily new in any absolute sense, perhaps only new for his particular patient—he is experimenting in his effort to relieve or cure the individual involved.[24] It could often be shown to be wrong to withhold such methods of trial. Such "experimentation" is, in principle, relatively uncomplicated. Great complications arise, however, when the experimentation on one patient is not expected to benefit the immediate patient but is for the good of patients in general. Recent increase in this type of experimentation requires consideration, for such a matter involves the most basic elements in the patient-physician relationship as well as the attitude toward life and its responsibilities of both the patient and the physician. As Guttentag [11] puts it, "not all experiments performed on men will ever be of value to these particular men. And it is with these breathing men that we are concerned as physicians."

Only physicians can legally take the responsibility for medical experimentation on man. In any case, no one else is so well equipped to carry out work "to confirm or disprove a biological generalization with regard to man . . . [than] the profession that is trained more completely than any other in comprehending the somatic and psychological aspects of human life, be it healthy or diseased." In addition to this reason there is another. As Guttentag [11] points out, it is related to the original patient-physician relationship: "Here *both* the healthy and the sick persons are . . . fellow-companions, partners to conquer a common enemy." Guttentag has called it "'mutual obligations of equals' or to use Weizsaecker's term, it is 'solidarity.' Objective experimentation to confirm or disprove some doubtful or suggested biological generalization is foreign to this relationship." He considers the physician-experimenter and the physician-friend as two distinct aspects of the doctor.

Against the background of the two roles played by the physician, Guttentag [11] considers three currently evolving developments. First, there is the use of force as exercised in Hitler's Germany. It seems unlikely that this will be of importance in this country, except for extremely rare local abuses, for the overwhelming majority of physician-experimenters, if not thoroughly aware of the nature of the original patient-physician relationship, are so deeply rooted in the democratic spirit that they agree, and will continue to agree, that the use of force is not justified on a single person, even if millions of other lives could be saved by such an act. They realize that as an amoral act from the standpoint of democratic brotherhood, it might create millions of amoral sequels, and that the moral history of mankind is more important than the scientific.

Second, the use of the "hopelessly incurable" as experimental subjects has developed recently. I have already stated the reasons for my deep conviction that those who are in imminent danger of death should not be subjected to experimentation, except as part of the therapeutic effort for the benefit of the subject himself. Occasionally, reports are found wherein use of the "hopelessly incurable" seems to justify dangerous experimentation. The error in this appears evident. It is not the physician's prerogative to make or to profit from such dubious judgments. The use of such subjects is meant to be noble in the democratic spirit, yet it unconsciously challenges this spirit more subtly but no less than the use of force, because it violates the concept of equality or brotherhood in violating the principle of the original patient-physician relationship. From the experimenter's point of view, the description "hopelessly incurable" is not germane to his purpose. The designation is inadequate, because it does not specify the time element—hopeless within hours, days, months, years? And if months or years are concerned, do all experts agree on the status of their respective sciences and deny the possibility of discovering effective agents within such a period? The term is also unnecessary. . . . From the standpoint of the physician-friend, the assertion is not germane to his purpose, either. To him it is an expression of detachment between physician and patient, the announcement of a scale of partnership *vs.* domination quite contrary to its original spirit. As a matter of fact, it creates the paradox that the healthier the patient, the more he should be the concern of his physician; the sicker, the less.[11]

Third, "increased technicalities of many problems and procedures" have arisen. To Guttentag [11] this suggests that for the protection of the subject the physician-friend and the physician-experimenter should be two persons, lest selfishness decide the issue. The physician-friend would play the part of attorney for the defense, whereas the physician-experimenter would be the prosecuting attorney. Practically, the physician-friend and the physician-experimenter must sometimes, and often will, be the same person. Nevertheless, it is necessary that the two attitudes be recognized and pondered.

Justification for Human Trial

The importance of the project undertaken must be commensurate with the risk involved. The insurance of this is a cardinal responsibility of all who undertake experimentation in man. However, there is still a vast area where judgment—one hopes sound judgment—must operate. Only the fanatic denies that animal experimentation must precede human experimentation. As Sir Geoffrey Jefferson [25] put it, "Man is too rare, too expensive, altogether too valuable an animal" to be first used in the study of technical procedures or trial of even therapeutic agents. There are, at the same time, species differences. Ultimately, the definitive test must be to undertake the study proposed. Medical research, when it involves treatment or any physical procedures beyond the simplest type, requires that the investigator or his close associate be a qualified physician. No other profession gives such prerogatives, and no other profession, probably, presents such a generally high level of unselfishness and compassion. Of these two qualities, unselfishness is the more important for subject and project alike. Imagination, objectivity, and the power to generalize soundly are all essential.

Responsibilities and Safeguards.—Claude Bernard[21] stated the responsibilities of the investigator as follows:

> As far as direct applicability to medical practice is concerned, it is quite certain that experiments made on man are always the most conclusive. No one has ever denied it. . . . First, have we a right to perform experiments and vivisections on man? Physicians make therapeutic experiments daily on their patients, and surgeons perform vivisections daily on their subjects. Experiments, then, may be performed on man, but within what limits? It is our duty and our right to perform an experiment on man whenever it can save his life, cure him, or gain him some personal benefit. The principle of medical and surgical morality, therefore, consists in never performing on man an experiment which might be harmful to him to any extent, even though the result might be highly advantageous to science, i. e., to the health of others. But performing experiments and operations exclusively from the point of view of the patient's own advantage does not prevent their turning out profitably to science.

Bernard's view cannot soundly be construed as ruling out risk when there is hope of gain; both must be weighed.

In patently nonhazardous experimentation, there is no necessity for the investigator to subject himself first to the experimental procedures. However, whenever doubt exists as to safety, it is advisable for the investigator first to subject himself to the possible hazards involved.

When it is not known whether a given treatment is likely to be effective, the investigator is entitled to withhold it if new and more promising therapy waits trial. However, he is not entitled to withhold therapy when its effectiveness is assured, except with the consent of the patient. Green states it thus: "where the value of a treatment, new or old, is doubtful, there may be a higher moral obligation to test it critically than to continue to prescribe it year-in-year-out with the support merely of custom or wishful thinking."[22] McCance has said: "the medical profession has a responsibility not only for the cure of the sick and for the prevention of disease but for the advancement of knowledge upon which both depend. This . . . responsibility can only be met by investigation and experiment."[20]

Although many differences exist between the practice of medicine and human experimentation, there are, nonetheless, certain parallels that can usefully be drawn in examining one's position of responsibility. In questions of malpractice a legitimate point is whether the actions of the physician were in accordance with generally accepted standards in the given case. So too the same question can be appropriately raised concerning experimentation.

> In research, standards must relate to how the investigator proceeded and how he checked himself. The means by which research of high quality has been managed and the safeguards employed to protect the subject can be generalized into a set of precepts similar to that governing malpractice, to serve as a guide. Thus, willful or negligent deviation, resulting in injury, would constitute a basis for liability. On the other hand, observance of all known precautions, even in the event of an untoward result, would protect the honest, qualified investigator. Neither he nor the physician is a guarantor of success, but each has a responsibility to his own law and credo.[6]

The responsibilities devolving on those who undertake experimentation in man are so great that, whenever even remote hazard is a possibility, group decision supported by a proper consultative body should be employed.[7] Self-experimentation "without such collaboration and consultation seems as indefensible as similar experimentation on another individual."[7] "At the Clinical Center of the National Institutes of Health, for instance, projects involving deviation from accepted medical practice or unusual hazard are presented in writing to a Clinical Research Committee. Consent is obtained from subjects and final approval from the Center's Medical Board and the Director of the National Institutes of Health."[6] The British Medical Research Council has said:

> In any particular case—so specialized has medical knowledge become—only a small group of experienced investigators, who have devoted themselves to this branch of medicine, are likely to be competent to pass an opinion on the advisability of undertaking any particular investigation. But in every branch of medicine such a group of investigators exists. It is upon them, and the specialized scientific societies to which they belong, that the medical profession must mainly rely for the creation of the body of precedents and the climate of opinion which shall guide investigators in clinical research . . . it is incumbent upon the medical scientific societies to accept this responsibility and, by encouraging critical discussion on the communications presented to them, help to resolve doubts and to form a body of opinion of what is necessary, desirable and justifiable to guide investigators in their field.[10]

Wiggers[9] has expressed a similar view.

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Types of Human Experimentation

These classifications can be considered from various points of view. For example, one scheme is based on the patient's role: (1) "passive," in which human tissues or products are examined, as by the pathologist or biochemist; (2) "late active," in which studies are applied to the patient only after prior investigation on animals; and (3) "initial active," in which work must be undertaken exclusively on man.[7] Another classification is based on the purpose of the research; that is, whether it is designed to be of value to the immediate patient under study or to patients in general. Still other categories of consideration are reasonable; for example, whether the investigation is to advance basic science or whether it falls into the realm of applied science.

The reviewer must confess to scant interest in such schemes. There are, however, several points that should be made, points which cut across various classifications.

1. Prior controlled experimentation in animals is absolutely essential whenever this is advantageous, and this is almost always, in one way or another, the case. Even when primary drug effects cannot profitably be studied in animals, possible toxic effects can and should be.
2. In certain circumstances, experimentation in animals is impossible or useless. For example, mental disease and its prodromal states must be studied in man. Studies of subjective responses, symptoms, require human subjects, although useful inferences can be drawn in some cases from animal work, for example, studies of the effect of analgesic agents on animal withdrawal reflexes presumably produced by pain. Since certain syndromes and diseases do not occur in animals, obviously they must be studied in man.
3. Although the investigator should be willing to serve as a subject in any project having even remote possibilities of hazard (as evidence of his good faith), self-experimentation is an unwise performance whenever judgment can enter into the conclusions drawn.
4. Any classification of human experimentation as "for the good of society" is to be viewed with distaste, even alarm. Undoubtedly all sound work has this as its ultimate aim, but such high-flown expressions are not necessary and have been used within recent memory as cover for outrageous ends.

Permissible vs. Nonpermissible Human Experimentation

Very often decision lies between two shades of gray.[26] When hazard is involved, or may be present, group decision by one's peers becomes important. Ivy[2] has presented some telling examples of rash or foolish experimentation. On top of all his other problems, the harassed investigator recognizes that sometimes to prevent an experiment may of itself be also an experiment, even a dangerous one.

Pope Pius XII[27] expressed the stand of the Roman Catholic Church thus:

> In the domain of . . . science it is an obvious law that the application of new methods to living men must be preceded by research on cadavers or the model of study and experimentation on animals. Sometimes, however, this procedure is found to be impossible, insufficient or not feasible from a practical point of view. In this case, medical research will try to work on its immediate object, the living man, in the interests of science, in the interests of the patient and in the interests of the community. Such a procedure is not to be rejected without further consideration. But you must stop at the limits laid down by the moral principles We have explained.

Propriety in Publication

When reports on human experimentation are prepared for publication,

> It cannot be assumed that it will be evident to every reader that the investigations being described were unobjectionable. Unless such is made unmistakably clear misconceptions can arise. In this connection a special responsibility devolves upon the editors, and editorial boards, of scientific journals. . . . It is desirable that editors and editorial boards, before accepting any communication, should not only satisfy themselves that the appropriate requirements have been fulfilled, but may properly insist that the reader is left in no doubt that such is indeed the case.[10]

There have been instances in which certain details and complications have been deleted from published reports to avoid unfavorable criticism. It seems unlikely that such abuses are common, but when they occur, it is probable that the study should not have been carried out in the first place. The failure to report serious complications in a final report is inexcusable.

Ethical and Moral Aspects

The physician, with his 2,500-year-old traditions and his constant preoccupation with problems of life and death, has understandably had a long concern with ethical matters. The first codification of such matters in the United States occurred in 1848,[28] when the American Medical Association patterned its statement on Sir Thomas Percival's "Medical Ethics" of 1803. The principal categories concerned the relationship of the physician to society, to his patient, and to his colleagues.

There have been a good many controversies involving medical ethics in the past 20 years. Fitts and Fitts[29] have suggested as various causes for this the splintering of medical knowledge into numerous specialties, leading as it does to group practice; the spread of insurance schemes, with intrusion of a third party between the physician and his patient; and finally "the radical treatment of serious disease, which appears, when first applied, to verge dangerously upon human experimentation." The implication of this last comment, i. e., the radical treatment of disease, however close to the legal stand it may be, is possibly at variance with present widespread humanitarian concepts.

Changes in ethical considerations may be slow, but they do occur and are illustrated in correspondence to the Royal Society in England. In 1756, Sir Hans Sloane described how,

> The princess Anne, now princess royal of Orange, falling ill of the small-pox in such a dangerous way that I very much feared her life, the late Queen Caroline, when princess of Wales, to secure her other children, and for the common good, begged the lives of six condemned criminals, who had not had the small-pox, in order to try the experiment of inoculation upon them. But Mr. Maitland, who had inoculated at Constantinople, declining for some reasons to perform the operation. . . . [but later he was persuaded and] undertook the operation, which succeeded in all but one, who had the matter of the small-pox put up her nose, which produced no distemper, but gave great uneasiness to the poor woman. . . . To make a further tryal, the late Queen Caroline procured half a dozen of the charity-children belonging to St. James' parish, who were inoculated, and all of them, except one (who had had the small-pox before, tho' she pretended not, for the sake of the reward) went thro' it with the symptoms of a favourable kind of that distemper.

The very fact that such a performance on the part of the present royal family of Great Britain would be unthinkable emphasizes the change.

This ethical change is further exemplified in recent correspondence to *Lancet*, in which the discussion, even though pros and cons are presented, indicates a lively conscience. In the letter which started this correspondence, Fisher[30] had this to say:

> It is a matter for regret that the use of normal children (or children suffering from some irrelevant disease) as controls in clinical research appears to be increasing.
>
> No medical procedure involving the slightest risk or accompanied by the slightest physical or mental pain may be inflicted on a child for experimental purposes unless there is a reasonable chance, or at least a hope, that the child may benefit thereby.
>
> If this is true—and I hope that there are few doctors in this country who would disagree—then it must surely be difficult to justify the use of two hydrocephalic infants reported in the paper by Dr. Doxiadis and his colleagues, and the use of a normal control by Dr. Bickel and his colleagues.
>
> It may be, of course, that there were some good reasons for the use of these children which have not been made clear.

Holt[31] replied for one group of authors:

> It is quite reasonable that Dr. Fisher should raise the question of the use of normal children or children suffering from some irrelevant disease as controls in clinical research. There are extreme opinions on both sides, but I feel most of us adopt a policy between the two—somewhere in the grey between the rather theoretical white and black. My own working policy, which differs slightly from that expounded by Dr. Fisher in the second paragraph of his letter, is that no procedure should be carried out involving risk or discomfort without a reasonable chance of benefit to that child *or other children;* and this principle was followed throughout our work. The crux of the matter is contained in the last sentence of Dr. Fisher's letter—we owe it to ourselves to explain our actions. Surely we all weigh these matters most carefully in our own consciences.

Further comment was made by Bickel and Gerrard:[32] "We are grateful to Dr. Fisher for raising a problem of which we are fully conscious in our daily work. Nevertheless, errors of metabolism constituting the underlying cause of many diseases cannot be understood or properly treated without knowledge of normal physiology."

Leys[33] commented on the previous correspondence:

> The privileged position which doctors hold in society depends entirely on the trust which people have in the purity of their motives. This is stated explicitly in the international code adopted by the World Medical Association in 1949: "Under no circumstances is a doctor permitted to do anything which would weaken the physical or mental resistance of a human being except from strictly therapeutic or prophylactic indications imposed in the interests of the patient." There is no justification here for risking an injury to an individual for the possible benefit to other people, as enunciated by Dr. Holt as his guiding principle. Such a rule would open the door wide to perversions of practice, even such as were inflicted by Nazi doctors on concentration-camp prisoners. The magnitude and crudity of their "experiments" must not be allowed to blunt sensitivity to breaches of the medical ethic made on a smaller scale and with greater plausibility. Of this nature are experiments performed upon condemned criminals, with or without the victim's consent, upon conscientious objectors to military service, upon persons with chronic mental illness or deficiency or incurable disease of any kind, and all procedures, whether therapeutic in intent or not, which are not designed with the sole intention of improving the lot of the individual upon whom they are performed. Only one exception can be allowed—i. e., when the experimental subject is an adult whose judgment is not impaired and who freely gives his consent. No child must ever be the subject of such an experiment.
>
> It is clear that the assumption by doctors of scientific methods and techniques calls for critical examination of the uses to which these methods are put. The scientific material of the clinical research-worker is human life.
>
> I should like to see a resumption of the practice by which all doctors upon qualification were required to make a declaration of adherence to the medical ethic. There is need for a revised, more simple form of the Hippocratic oath, relevant to the circumstances of the 20th century. For some time the ethics subcommittee of the Medical Association for Prevention of War has been occupied with such a revision, and I give, for the sake of discussion, the tentative and interim results of this attempt.

Items (2) and (4) of the revised oath are pertinent to the present discussion:

> (2) To direct all my work to the preservation of life and the relief of suffering, and under no circumstances whatever to use my medical knowledge to harm any person, nor take part in any experiment involving risk of injury, without assuring myself of the understanding and freely given consent of an adult subject, nor without consulting my colleagues upon the value and necessity for such an experiment.
>
> (4) To communicate freely to all doctors any discoveries which I believe myself to have made concerning the nature, cure, or prevention of disease.

Ethical and moral implications and problems surround every facet of experimentation in man. This has been evident in each of the preceding sections of this report. The central conclusion is that it is unethical and immoral to carry out potentially dangerous experiments without the subject's knowledge and permission. Every act of a physician designed soundly to relieve or cure a given patient is experimentation of an easily justifiable kind. The patient's placement of himself in the physician's hands is evidence of consent. The problem becomes a knotty one when the acts of the physician are directed not toward benefit of the patient present but toward patients in general. Such action requires the explicit consent of the informed patient. It also requires more than this—it requires profound thought and consideration on the part of the physician, for the complexities of medicine are, in some cases, so great that it is not reasonable to expect that the patient can be adequately informed as to the full implications of what his consent means. His trust in the physician may lead him too easily to say yes.[34] Although there is no excuse for failure to do one's best to present an accurately informative picture to the subject, it is an injunction to the experimenter himself to cultivate a deep sense of his own responsibility in such a case.

"The patient, however humble and however ill, in whatever degree derelict and forlorn, has sacred rights which the physician must always put ahead of his burning curiosity." [3] The situation is a safer one, as Guttentag points out, when the "physician-friend" who looks after the patient's illness and welfare in general is not the same person as the "physician-experimenter."

"The ethical principles involved in the use of the mentally incompetent are the same as for mentally competent persons. The only difference involves the matter of consent. Since mental cases are likened to children in an ethical and legal sense, the consent of the guardian is required." [2]

The ethics and practice of placebo therapy have been reviewed and discussed in considerable detail by Leslie [35] who concluded, "The proper use of the placebo requires, in addition to broad medical knowledge, a depth of human understanding not requisite to the purely materialistic approach to medicine."

In a speech delivered on Sept. 14, 1952, Pope Pius XII [27] discussed the moral limits of medical research and treatment and, in particular, the interests of science as justification for research and the use of new methods. If a procedure "cannot be used without injuring the rights of others or without violating some moral rule of absolute value . . . morally the method is not admissible," even though knowledge might be increased by its use. The reason for this is that, just as science is not the highest good, so also the desire for scientific growth cannot override certain moral values. "Science itself, therefore, as well as its research and acquisition, must be inserted in the order of values."

Further discussion by the Pope concerned the interests of the patient as justification of new medical methods of research and treatment. The physician's rights or power over the patient or subject are only those given by the subject, bearing in mind that "the patient cannot confer rights he does not possess." According to this philosophy, "The patient, then, has no right to involve his physical or psychic integrity in medical experiments or research when they entail serious destruction, mutilation, wounds or perils."

A third interest is the *bonum commune* or common good. The two interests already discussed, that of science and that of the patient, are closely allied to the general interest. This leads to the question, "Can public authority, on which rests responsibility for the common good, give the doctor the power to experiment on the individual in the interests of science and the community in order to discover and try out new methods and procedures?" The answer is obviously "no,"[27] for the individual must not be subordinated to the community; the community exists for the man.

Legal Considerations

The legal considerations surrounding human experimentation have been exhaustively reviewed and documented by Ladimer.[36] Appropriate to the present report is a statement of the basic assumptions and general principles involved. In addition to this, attention will be called to some surprising lacks of legal precedent in this field.

The practice of medicine has been described over some thousands of years in recorded history, and during this vast period it has been hedged about with innumerable oaths, precedents, customs, rules, orders, and laws for the protection of the patient. Human experimentation is as ancient as the practice of medicine; yet, remarkably enough, no specified legal precedents have been set down to protect the subject or the investigator. At the same time there is an abundance of precedent to indicate that, however able, skillful, conscientious, well trained, and generally well qualified the investigator is, he experiments on man to his peril. The first malpractice suit involving alleged experimentation occurred in 1767, *Slater* v. *Baker*. It "established the rule that experimentation was at the physician's peril," [36a] although the court commented at the time on the surgeon's good character and repute.

As Ladimer [36a] has put it, the position taken by strict legal writers and jurists who have summarized the issue's present position is as follows: In treating the patient "there must be no experimentation . . .

we find that legal encyclopedias have unwaveringly set forth that while it is the duty of the physician or surgeon to keep up with advancements in his profession, it is also his duty not to try to forge ahead of it by trying experiments." The doctrine is: "The physician experiments at his peril." Many similar examples could be given. In this seemingly harsh stand "the law" seems to close its eyes to reality, for, as every able physician knows, the adequate practice of medicine involves continual experimentation. No two patients respond precisely alike to any therapeutic procedure. Even in ordinary practice the able physician experiments until his treatment is successful or the patient dies.

The precedent and interpretations just mentioned have to do with the comparatively simple situation of experimentation designed to benefit the immediate patient. The important but much more difficult situation remains, and is scarcely mentioned in legal discussion, in which the research is not designed to benefit the immediate patient but rather patients in general.

To a layman like myself, this is an instance in which the law and its interpretation are far removed from actual practices and from current, universally accepted ethical and moral concepts of Western civilization.[36a] These concepts can be summarized as follows: 1. Progress in the medical sciences depends upon research. 2. Much of this research requires human experimentation. 3. Human experimentation is necessary and proper. 4. It is not considered just that a man be placed in jeopardy or penalized for helping his brother.

The need for a redefinition of human experimentation becomes apparent, because many court rulings equate experimentation with "rash action" and "ignorant and unskillful departure from approved methods." The low esteem of the court for such experimentation is expressed in such phrases as "rash or experimental methods," "mere experiment," or "reckless experiment." By no means could all the acts so castigated be labeled as foolish, nor were they always the work of incompetents. The remarks quoted, "quite typical in cases of this kind reveal[s] the association in the judicial mind between experimentation and professional disregard or negligence. Needless to say, this represents either a complete misconception of scientific experimentation or the singular use of the term so that it partakes of reckless behavior or quackery. . . . The term 'experimentation' has been used loosely by the courts," so says Doctor of Jurisprudence Ladimer, as I would scarcely dare to do. He points out that the precedents, the cases of record, have "dealt not with major problems baffling to medicine and science on which basic research or applied clinical study was required, but with questions which confront the regular practitioner."

In his superb review Ladimer[36a] has said:

> The term "experimentation" must be considered objectively (preferably discarded if it retains the connotation of improper medical practice) so that it is recognizable as a legitimate scientific endeavor which can be advanced by the recognized research scientist. The legal issue would then become not experimentation versus accepted practice of the art of medicine but an evaluation of the plan and conduct of research in relation to specific fact situations, that is, whether the research was conducted with due regard to the interests of the subject. The law has a duty to comprehend the scope and elements of diverse human activity and their places in society if it is to assist in making individual judgments and setting or recognizing general values. . . . Essentially, medical research on human beings consists in experimentation, that is, deliberately inducing or altering body or mental functions, directly or indirectly, in individuals or in groups primarily for the advancement of health, science and human welfare.

Continuing, Ladimer[36a] has maintained that medical research

> is significantly different from medical practice in such respects as purpose and attitudes, scientific problem or medical hypothesis, study design or treatment, relative obligations of physician-researcher and patient-subject and general environment including scientific staff, facilities and types of clinical material selected. . . . The conduct of medical practice, generally conceived to be diagnosis, treatment and care, is governed by state statute and supporting administrative licensing and regulatory bodies. Medical research on human subjects, except as it is an inherent but not predominant incident of such practice, would appear to be outside the scope of [medical practice]. . . . There is no existing broad police power statute for control of human research although it is, by its nature, subject to the general police power.

Human research "today warrants [legal] recognition as a separate endeavor affected with a public interest as significant as medical practice itself."

Codes

As already mentioned, it is not my view that many rules can be laid down to govern experimentation in man. In most cases, these are more likely to do harm than good. Rules are not going to curb the unscrupulous. Such abuses as have occurred are usually due to ignorance and inexperience. The most effective protection for all concerned depends upon a recognition and an understanding of the various aspects of the problem. Eventually, the broad gap between the law of the land and its interpretation, on the one hand, and scientifically, ethically, and morally sanctioned experimentation in man, on the other hand, must be narrowed, if not closed. This legal development can be helpful and directed toward progress or can be harmfully restrictive. Which it shall be will be determined by the breadth of understanding expended on this complex subject.

Since only physicians can accept the responsibility for human experimentation, beyond the simplest procedures, the oath of Hippocrates has been a basic guide. The physician agrees to work to the best of his ability for the good of his patients and to "abstain from whatever is deleterious and mischievous." As Claude Bernard[21] put it a century ago: In the field of experimentation "Christian morals forbid only one thing, doing ill to one's neighbor." In terms of principle, these elevated sentiments possibly say all that is necessary. The writer, in common with many other investigators, has sought a practical spelling-out of the principle involved. Various attempts to do this will now be described, using as the basic framework for discussion the 10 points developed at the Nuremberg Military Tribunals.[37]

Nuremberg Code's 10 Points.—It is puzzling to me, as a layman in legal matters, why the opinions expressed and the judgments rendered by the Nuremberg Military Tribunals concerning human experimentation cannot be construed as legal precedents (evidently not the case, cf. Ladimer[36a]) when they say that "certain basic principles must be observed in order to satisfy moral, ethical and legal concepts." At any rate, violation of these principles was considered as sufficient basis for imposing seven death sentences and nine prison terms. It would not seem unreasonable to conclude that, if "certain basic principles" (to be stated), are "satisfied," then "legality" shall have been attained. However that may be, the principles and the discussion of them are as follows.[37]

> Nuremberg Rule 1: *The voluntary consent of the human subject is absolutely essential.*
>
> This means that the person involved should have legal capacity to give consent; should be so situated as to be able to exercise free power of choice, without the intervention of any element of force, fraud, deceit, duress, over-reaching, or other ulterior form of constraint or coercion; and should have sufficient knowledge and comprehension of the elements of the subject matter involved as to enable him to make an understanding and enlightened decision. This latter element requires that before the acceptance of an affirmative decision by the experimental subject there should be made known to him the nature, duration, and purpose of the experiment; the method and means by which it is to be conducted; all inconveniences and hazards reasonably to be expected; and the effects upon his health or person which may possibly come from his participation in the experiments.
>
> The duty and responsibility for ascertaining the quality of the consent rests upon each individual who initiates, directs or engages in the experiment. It is a personal duty and responsibility which may not be delegated to another with impunity.

On first reading, this sounds simple, straightforward, and absolutely to the point. Reflection reveals certain difficulties. For one thing, a rigid interpretation of this would effectively cripple, if not eliminate, most research in the field of mental disease, which is one of the two or three greatest medical problems. However, Ivy served as chief medical consultant to the War Crimes Trials and presumably had a hand in formulating the 10 points. As he has said previously: "The ethical principles involved in the use of the mentally incompetent are the same as for mentally competent persons. The only difference involves the matter of consent. Since mental cases are likened to children in an ethical and legal sense, the consent of the guardian is required."[2] If this were the intention of the Nuremberg Tribunal, it is regrettable that the matter was not explicitly stated, for more and more the 10 points are referred to as a sort of Western credo.

We can consider what may be other difficulties in the way of widespread acceptance, difficulties not with the spirit and principal substance of the 10 points but difficulties, nonetheless, of interpretation.

Strict observance of point one would cast considerable doubt not only on the propriety of studying mental disease but also on the use of placebos, essential to progress in studies in which judgment is involved in decision.[38] Explicit observance of point one would require detailed explanation to the participating subject with the inevitable result that he would become self-conscious and introspective. An abundance of evidence in the field of study of subjective responses has shown that such introspection has produced misleading results.[5] The use of placebos in therapy, occasionally necessary for the guidance of the able, responsible physician as well as the treatment of the patient, could hardly be tolerated under a strict observance of the point in question.[9]

Furthermore, how is the investigator to draw a practical line in the prior information to be given his patient, between "reasonably to be expected" and possible hazards, when these will often be quite unknown in first experiments? Kety's[8] discussion of this question is, as usual, to the point:

> In studies on normal individuals where there was no intent or little possibility of helping the subject, the rule of voluntary consent is, of course, absolutely essential and the necessity of complete explanation equally important. The completeness of the explanation, however, need refer only to that information which will enable the subject to make a judgment upon hazards and need not include other scientific information irrelevant to the question of risk and knowledge of which on the part of the subject may be prejudicial to a controlled experiment. In other words, if one were giving a potent drug or a placebo, it would be necessary to explain to the subject only the risks involved in the taking of the drug. In the case of patients there are important justifications for clinical research in addition to those which hold for normal controls. In the first place, if the research is relevant to the clinical condition from which the patient is suffering, and I feel that it should be, there is the clear possibility of personal benefit to the patient from the research itself, and there, perhaps, the criterion might be the chance of harming the patient versus the chance of helping him. Even though both of these chances may be low, in most clinical research the chance of personal benefit is usually considerably greater than the chance of harm to the individual patient.

> With regard to the justification for using a placebo instead of a drug in the treatment of a disease, this can, of course, be justified if the purpose of the study is to evaluate a new and untried drug, since one can hardly be criticized for withholding an agent of unknown potential for good or harm. With regard to the question of withholding a drug of known benefit temporarily, the concept of greater harm versus greater good to the patient may still apply, in addition to which it may be perfectly possible to get the voluntary consent of the patient to cooperate in a research problem in which certain parts of the treatment may be delayed or withheld temporarily in order to make certain observations. In fact, in any case where the element of hazard is greater than the chances of benefit, the patient may still consent with full knowledge of the risk.

When a patient places himself in the hands of a physician for relief or cure of a symptom or disease, this act implies consent to the physician to carry out the necessary acceptable means to relieve or cure. If the problem is pain, for example, we know that a placebo will often relieve one-half to two-thirds of the pain relievable with an optimal dose of morphine.[39] Surely it would be carrying matters too far to require a dissertation to the patient on grades or degrees of relief anticipated, when real value could be expected from the use of a placebo. Such use of a placebo could reveal, for example, whether a powerful narcotic was actually necessary or not.

Possibly in the beginning, before its power to relieve was established, the use of a placebo in such work might have been challenged on ethical grounds more effectively than at present. This is true of many, if not most, standard therapeutic procedures in wide use today. In the early days of cardiac catheterization, that procedure could have been challenged on serious grounds as jeopardizing the immediate subject's life. Subsequently this has indeed been proved at times to be the case. At present, it is widely recognized that the demonstrated value of the technique outweighs the risk and this has been recognized by the award of a Nobel prize. Ladimer [39a] has described in chilling detail the probable fate in a court of law of the conscientious but bold investigator who takes such risks and experiences his failures early. In most cases, neither true risk nor benefit can be known early, and therefore they cannot be adequately described.

It is easy enough to say, as point one does, that the subject "should have sufficient knowledge and comprehension of the elements of the subject matter involved as to enable him to make an understanding and enlightened decision." Practically, this is often quite impossible, as we have seen, for the complexities of essential medical research have reached the point where the full implications and possible hazards cannot always be known to anyone and are often communicable only to a few informed investigators and sometimes not even to them. Certainly the full implications of work to be done are often not really communicable to lay subjects. As mentioned in an earlier section, this throws a serious burden on the responsible investigator. Once again, point one states a requirement very often impossible of fulfillment.

A further limitation on the matter of consent, as viewed by the Roman Catholic Church, has been expressed by Pope Pius XII [27]:

> In the first place it must be assumed that, as a private person, the doctor can take no measure or try no course of action without the consent of the patient. The doctor has no other rights or power over the patient than those which the latter gives him, explicitly or implicitly and tacitly. On his side, the patient cannot confer rights he does not possess. In this discussion the decisive point is the moral licitness of the right a patient has to dispose of himself. Here is the moral limit to the doctor's action taken with the consent of the patient.
>
> As for the patient, he is not absolute master of himself, of his body or of his soul. He cannot, therefore, freely dispose of himself as he pleases. Even the reason for which he acts is of itself neither sufficient nor determining. The patient is bound to the imminent teleology laid down by nature. He has the right of *use*, limited by natural finality, of the faculties and powers of his human nature. Because he is a user and not a proprietor, he does not have unlimited power to destroy or mutilate his body and its functions. Nevertheless, by virtue of the principle of totality, by virtue of his right to use the services of his organism as a whole, the patient can allow individual parts to be destroyed or mutilated when and to the extent necessary for the good of his being as a whole. He may do so to ensure his being's existence and to avoid or, naturally, to repair serious and lasting damage which cannot otherwise be avoided or repaired.
>
> The patient, then, has no right to involve his physical or psychic integrity in medical experiments or research when they entail serious destruction, mutilation, wounds or perils.
>
> Moreover, in exercising his right to dispose of himself, his faculties and his organs, the individual must observe the hierarchy of the orders of values—or within a single order of values, the hierarchy of particular rights—insofar as the rules of morality demand. Thus, for example, a man cannot perform on himself or allow doctors to perform acts of a physical or somatic nature which doubtless relieve heavy physical or psychic burdens or infirmities, but which bring about at the same time permanent abolition or considerable and durable diminution of his freedom, that is, of his human personality in its typical and characteristic function. Such an act degrades a man to the level of a being reacting only to acquire reflexes or to a living automaton. The moral law does not allow such a reversal of values. Here it sets up its limits to the "medical interests of the patient."

Brig. Gen. Telford Taylor,[40] who served as chief counsel for the prosecution of war criminals, says of the 10 points from the Nuremberg Trials that "the judgment lays down ten standards to which physicians must conform." Must? Most investigators would if they always knew how. Some of the foregoing discussion might be labeled as quibbling, but some is not. "The law is not concerned with trifles." It is at times difficult to distinguish between the two in a matter of this kind. Nothing said in this discussion should be construed as an attack on the principle of consent. The discussion is set down to indicate that even the "obvious" matter of consent is not so easy to live up to as it sounds.

Nuremberg Rule 2: *The experiment should be such as to yield fruitful results for the good of society, unprocurable by other methods or means of study, and not random and unnecessary in nature.*

The somewhat unsavory nature of the phrase "for the good of society" has been discussed previously. Point two is vague and frowns on random experiments; however, anesthesia, x-rays, radium, and penicillin, to mention a few products of "random" experimentation, seem to justify the disallowed approach. Most of the epoch-making discoveries in science have been unexpected.[41] Surely there is something to be said for the "random" experiment. I, at least, would not know how to define experiments "unnecessary in nature." Doubtless cardiac catheterization and frontal lobotomy would each have been placed in such a category at the beginning of their use. Perhaps lobotomy would be characterized by many in this way now, although it would not have been a few years ago. Decision is difficult; experiment clearly perilous.

Nuremberg Rule 3: *The experiment should be so designed and based on the results of animal experimentation and a knowledge of the natural history of the disease or other problem under study that the anticipated results will justify the performance of the experiment.*

But if the anticipated results fail to justify the performance of the experiment, has the investigator necessarily been guilty of wrong behavior? Who can guarantee the success of any new experiment?

The aforementioned comments are by no means intended to scoff at this valiant effort to codify permissible experimentation in man. They are intended, rather, to indicate more clearly than the 10 points do how difficult it is to be precise in this field. The remaining seven points will be set down without comment.

Nuremberg Rule 4: *The experiment should be so conducted as to avoid all unnecessary physical and mental suffering and injury.*

Nuremberg Rule 5: *No experiment should be conducted where there is an* a priori *reason to believe that death or disabling injury will occur; except, perhaps, in those experiments where the experimental physicians also serve as subjects.*

Nuremberg Rule 6: *The degree of risk to be taken should never exceed that determined by the humanitarian importance of the problem to be solved by the experiment.*

Nuremberg Rule 7: *Proper preparations should be made and adequate facilities provided to protect the experimental subject against even remote possibilities of injury, disability, or death.*

Nuremberg Rule 8: *The experiment should be conducted only by scientifically qualified persons. The highest degree of skill and care should be required through all stages of the experiment of those who conduct or engage in the experiment.*

Nuremberg Rule 9: *During the course of the experiment the human subject should be at liberty to bring the experiment to an end if he has reached the physical or mental state where continuation of the experiment seems to him to be impossible.*

Nuremberg Rule 10: *During the course of the experiment the scientist in charge must be prepared to terminate the experiment at any stage, if he has probable cause to believe, in the exercise of good faith, superior skill and careful judgment required of him that a continuation of the experiment is likely to result in injury, disability, or death to the experimental subject.*

Notwithstanding the difficulties of formulating rules to cover all occasions, it was clear from the principles set down at Nuremberg[37] that during the war

> these ten principles were much more frequently honored in their breach than in their observance. Many of the concentration camp inmates who were the victims of these atrocities were citizens of countries other than the German Reich. They were non-German nationals, including Jews and "asocial persons," both prisoners of war and civilians, who had been imprisoned and forced to submit to these tortures and barbarities without so much as a semblance of trial. In every single instance appearing in the record, subjects were used who did not consent to the experiments; indeed, as to some experiments, it is not even contended by the defendants that the subjects occupied the status of volunteers. In no case was the experimental subject at liberty of his own free choice to withdraw from any experiment. In many cases experiments were performed by unqualified persons; were conducted at random for no adequate scientific reason, and under revolting physical conditions. All of the experiments were conducted with unnecessary suffering and injury and but very little, if any, precautions were taken to protect or safeguard the human subjects from the possibilities of injury, disability, or death. In every one of the experiments the subjects experienced extreme pain or torture, and in most of them they suffered permanent injury, mutilation, or death, either as a direct result of the experiments or because of lack of adequate follow-up care.

Declarations of Geneva and Rome.—The declarations of Geneva and Rome, which have been adopted by the World Medical Association, consist of a rephrasing and amplification of the Hippocratic oath.[42] Nothing is said directly about experimentation; however, in the section on "Duties of Doctors in General," the following statement could be considered as a limitation of experimentation: "Under no circumstances is a doctor permitted to do anything that would weaken the physical or mental resistance of a human being, except for strictly therapeutic or prophylactic indications imposed in the interest of the patient."

Views of the United States Public Health Service.—The United States Public Health Service has, in effect, adopted the Nuremberg Code's 10 points, with added comment on the importance of group review and group approval of all procedures when even remote possibilities for hazard exist.[7] The rights and welfare of the patient are emphasized.

Concerning research patients at the Clinical Center for Medical Research of the United States Public Health Service, Topping[43] has said:

> An overriding principle governing our clinical studies is that the welfare of individual human beings takes precedence over every other consideration. Medical procedures or therapy substantially different from accepted general medical practices are often an essential component of clinical medical

> research. This offers the only means of acquiring certain information necessary to solve the problems of the diseases and disorders that afflict man. Ethical and scientific considerations dictate, however, that these investigations must be undertaken only after mature thought, under rigorously defined and controlled conditions, and under circumstances that will minimize the dangers of predictable or unpredictable hazards. The basic principle on which all such investigations must rest is that human beings have inalienable rights that supersede all other considerations that may be raised in the name either of science or of the general public welfare. The responsibility of the physician for the physical and mental well-being of persons in his care and for observance of the ethics of his profession cannot be overridden by any element of study or research that is interjected into the relationship between the physician or surgeon and persons in his care.

Views of French Academies.—The National Academy of Medicine, of France,[44] points to the need for a distinction between (1) investigation and therapy directed toward the patient's health as the right and duty of the physician, "conducted with the necessary prudence and following the rules of medical ethics," and (2) research with other ends in view. In this case, in which the experimentation is "for scientific purposes only" it is essential that (1) only true volunteers who are informed concerning the project be used and that (2) the investigators be well qualified for the task at hand and thus reduce the hazard to a minimum.

The view of the French Academy of Moral and Political Sciences is that only responsible, experienced scientists should engage in human experimentation, men who can be expected to draw their own prudent limits to their activities, for written law of itself cannot provide an adequate safeguard. The final justification for such work is the scientific knowledge gained.[45]

British Views.—British views on this subject have been stated by J. M. Mackintosh,[46] a British scientist acting as special consultant to the United States Public Health Service. He has made the following points: Consent is essential by the individual or his guardian.

> The law in England is by no means clear as to the responsibility of the experimenter in the case of accident arising. The maxim "volenti non fit injuria" still holds, and might be freely expressed as "volunteers can't claim damages." But, of course, experimental research on sick persons designed to elucidate the nature of their disease and to provide treatment is well established. There has been a movement of late, however, to invite sick persons to cooperate in physical experiments upon themselves with the primary object of elucidating some fundamental problem of disease, without necessarily affecting their individual treatment. [Mackintosh points out that the consent] of a patient as a member of a research team acting as it were the part of the donor in the experiment, is new and startling. . . . Whether this cooperation in the event of accident is covered by the consent in writing of the patient is a matter which would have to be tested in the courts. Obviously the patient would be protected in common law here, as elsewhere, against negligence. But suppose no negligence has occurred, and in consequence of an experiment—the outcome of which cannot be known—a patient suffers a damage or death. The position of the director of the team and of its members would stand in some doubt. It is clear that the law would have to require 1) that the patient had been clearly informed of the nature and purpose of the experiment and of any results that it might involve; 2) that the experiment had been carried out not merely without negligence but with every available precaution against disaster, (e. g., by the provision of restorative apparatus); and 3) that the person responsible for the experiment was a person who could in the eyes of the law be confidently entrusted with the important tasks which he was undertaking. In this respect, it is evident that in addition to any expertly qualified scientist, a physician of standing would have to subscribe to the responsibility of the team.

Mackintosh [46] recognizes two ways of safeguarding the patient after the aforementioned propositions are accepted. This can be either by "an elaborate and meticulously worded code of regulations designed to cover the whole pattern of situations which might occur," or, abandoning any attempt to use a code of regulations, by the use of a "carefully worded 'statement of faith' on the ethical question of research." He expresses as his personal view that "the mere preparation of a closely defined code of regulations would defeat its own purpose. Human beings are not alike, and a code of regulations obeyed to the letter by one research worker might well result in irretrievable damage of a patient. There is no code that could cover the frailties of an inefficient worker, or the sinister vagaries of a research student who placed his own ambitions above the human needs and rights of the patient."

The British Medical Research Council [10] has also said, "it is impossible to frame a code of general advice which would adequately cover the ever changing circumstances which arise."

Views of the Roman Catholic Church.—Pope Pius XII [27] has said:

> Sometimes it happens that a method cannot be used without injuring the rights of others or without violating some moral rule of absolute value. In such a case, although one rightly envisages and pursues the increase of knowledge, morally the method is not admissible. Why not? Because science is not the highest value, that to which all other orders of values—or in the same order of value, all particular values—should be subordinated. Science itself, therefore, as well as its research and acquisitions, must be inserted in the order of values. Here there are well defined limits which even medical science cannot transgress without violating higher moral rules. The confidential relations between doctor and patient, the personal right of the patient to the life of his body and soul in its psychic and moral integrity are just some of the many values superior to scientific interest. This point will become more obvious as We proceed.
>
> Without doubt, before giving moral authorization to the use of new methods, one cannot ask that any danger or any risk be excluded. That would exceed human possibilities, paralyze all serious scientific research and very frequently be to the detriment of the patient. In these cases the weighing of the danger must be left to the judgment of the tried and competent doctor. Nevertheless, as Our explanation has shown, there is a degree of danger that morality cannot allow. In doubtful cases, when means already known have failed, it may happen that a new method still insufficiently tried offers, together with very dangerous elements, appre-

ciable chances of success. If the patient gives his consent, the use of the procedure in question is licit. But this way of acting cannot be upheld as a line of conduct in normal cases.

People will perhaps object that the ideas set forth here present a serious obstacle to scientific research and work. Nevertheless, the limits We have outlined are not by definition an obstacle to progress. The field of medicine cannot be different in this respect from other fields of man's research, investigations and work. The great moral demands force the impetuous flow of human thought and will to flow, like water from the mountains, into certain channels. They contain the flow to increase its efficiency and usefulness. They dam it so that it does not overflow and cause ravages that can never be compensated for by the special good it seeks. In appearance, moral demands are a brake. In fact, they contribute to the best and most beautiful of what man has produced for science, the individual and the community.

Requirements of the American Medical Association.—The American Medical Association[18a] has three principal requirements: "(1) the voluntary consent of the person on whom the experiment is to be performed; (2) the danger of each experiment must be previously investigated by animal experimentation, and (3) the experiment must be performed under proper medical protection and management." This is, in essence, similar to the Nuremberg document, and the comments appended to that are pertinent here.

Wiggers' Statements.—In effect, Wiggers[9] restated the 10 points of the Nuremberg Code, with extensions or additions as follows:

1. Human experiments should not be projected until their necessity has been unquestionably established and a feasible humane procedure for their conduct has been formulated.

2. The scientific, ethical, and legal considerations pertaining to contemplated studies on human subjects should, whenever possible, be reviewed and approved by a group of colleagues who will not participate in the investigation. The nature of the experiments and reasons for their performance should be explained.

8. The investigation should be so conducted that legal liability under malpractice or personal injury laws never comes into question.

To follow Wiggers' point one concerning necessity would, of course, be proper if danger attended the proposal. In experiments devoid of hazard it is difficult to see why the experimenter should not have freedom to try out his hunches, provided that the subjects understand the uncertain nature of the project and give consent. Many of the great discoveries of science have come from just such "unnecessary" and "random" experimentation.[41] Regarding point eight, as the laws are now written and at present interpreted,[38a] it seems clear that the investigator is frequently, if not always, in danger of being subjected to "legal liability under malpractice or personal injury laws."

World Medical Association.—The World Medical Association has presented a summary of a long report prepared by the Public Health Council of the Netherlands, which was submitted to that country's Minister of Social Affairs and Health on Oct. 10, 1955. After defining human experimentation as any "intervention in the psychic and/or somatic integrity of man which exceeds in nature or extent those in common practice," the report presents an elaborating discussion and summary of reasonable practices already discussed.

Approval of the Subject. It is generally agreed that if the experiment is not solely, primarily, or to any degree a direct benefit to the subject, his approval is required. This approval should neither be conditioned by idealistic impulses, (nurses and medical students); nor by special conditions, (prisoners, etc.). Even under ideal conditions, the subject's consent has only relative importance.

However the committee felt that when a physician undertakes "new treatment" on his own patient, the relationship of confidence between physician and patient is in no way violated if the physician increases his knowledge or experience without first informing the patient, with the understanding that recovery is not delayed and there is no detrimental effect.

After all, hospitals exist not only to treat patients, but also to increase medical knowledge and skill. Animal experimentation always precedes that on humans. The public should understand that the interests of the patients require a certain amount of experimentation.

Risk. "Risk" is defined as "any danger that is greater than the inevitable peril." Surgical procedures inevitably involve a risk, therefore, proper investigation and use of powerful new medicaments cannot be carried out without a degree of inevitable risk to the patient.

A distinction is made between the research expert and the investigator who is also the patient's attending physician. The Committee was of the opinion that "medical activities involving risk to the experimental subject should not be carried on by the practicing physician; the practicing physician who also is the investigator is not the person qualified to objectively judge the risk involved."

When experimentation is conducted in institutions such as homes for children, convalescents or old people, etc., the responsibility must be shared by the attending physician in addition to the investigator.

The Committee recognizes the inherent right of a person to accept a voluntary risk, and the right of the investigator to make use of this attitude to achieve altruistic objectives but ethics must act as a check wherever a great risk is involved. Dangerous experiments are never justifiable if the aim is only advancement of medical knowledge; they must also entail some benefit for humanity.

The Committee recognized that in time of war or epidemic, dangerous experiments may be justified. However, in normal times, "human experiments involving dangerous risks of life cannot be reconciled with the nature and objective of the medical profession." Hence it recognized that the nature of this problem does not make it possible to have clearly defined standards governing experimentation; "the conscience of the investigator will have to determine the course of conduct" and even the "individual conscience cannot be relied upon unconditionally." . . . For, "scientific experimentations demand from the investigator an objective attitude, a certain distance and restraint toward his object of experimentation which is actually in conflict with the relationship of physician and patient."

Standards. Nevertheless, it is felt that standards should be sought that will govern individual conscience in making decisions; guarantee acceptable scientific procedures; and provide all the precautions necessary.

The Committee recommends the following guarantees and standards:

- a. Study of relevant publications to avoid unnecessary repetitions of experiments;
- b. The physicians conducting experiments should have special knowledge of the problem and be completely responsible;
- c. Good organization and execution;
- d. Every available aid for special or emergency treatment of the experimental subject should be available.

Prior to experimentation the following aspects should be considered:

1. Can the experiment, wholly or partly, be carried out on animals?
2. What is the minimum requirement to obtain the observation? Is its importance and durations ethically justifiable?
3. What is the minimum requirement in altering the conditions of the experiment?
4. Are the requirements for the observation and the alterations of conditions the same?
5. What arrangements are planned? Is the project the fruit of mature thought and expert advice?
6. How will the results be used in obtaining a definite *conclusion?*

Risk, inconvenience or pain for the subject should be governed by these prinicples:

- a. The investigator's responsibility is more important than the willingness of the subject to accept the conditions;
- b. The investigator should consult other experts on the research project in order to intensify the sense of responsibility;
- c. The subject must be fully informed and must consent freely;
- d. If considerable risk is involved, the experiment is not in accord with the object and purpose of medicine;
- e. A practicing physician should not become an investigator on his own patient, if the experiment involves danger. A body of advisers should be consulted;
- f. Experiments should be discontinued if the subject so desires or if unexpected danger is encountered, activities the consequences of which cannot be undone, and which therefore cannot be discontinued, are therefore disapproved;
- g. Any suffering or danger not strictly inevitable must be prevented;
- h. Experiments on children; in institutions for children, old people, etc.; on the insane; or on prisoners, which involve dangerous risks, inconvenience or pain are not approved. All experiments on the dying under any circumstance are disapproved;
- i. The "utmost restraint" must be exercised in experiments on patients deemed to have an incurable malady, even though they volunteer as subjects;
- j. Unnnecessary examinations should be avoided, and diagnostic activities that may be dangerous are justified only if they result in effective therapy. In routine examinations new methods that are dangerous should be strictly limited.

The following additions are suggested: 1. Patients who are soon to die or who are in imminent danger of death should not be considered suitable subjects for research unless it is intended to benefit themselves. Potentially useful procedures might thus be unjustly blamed and the reputation of the investigator be damaged. 2. As a general principle, subjects with an unrelated disease should not be utilized for investigation involving another disease.

The principle codes have been presented above. The armed services in the United States and one or two state organizations abroad have classified codes which cannot be quoted. Such codes as I have seen do not contain anything not presented here.

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PORENCEPHALY.—The term porencephaly is used to indicate nontumorous cystic lesions of the brain communicating with the ventricles and/or the subarachnoid space, resulting from either developmental or destructive lesions. It is not possible to assign each case to one or the other pathogenic group on a clinical basis. The large majority of the cases presented belong to the group of destructive lesions, or "encephaloclastic porencephalies." . . . The cases in which symmetrical bilateral frontal cysts were demonstrated is the only one which can reasonably be considered as belonging to the developmental, or "schizencephalic," group. We have limited the use of the term porencephaly to those cases in which the etiological lesion occurred prior to, incidental to, or shortly after birth. The clinical features of porencephaly as a disease consist, in a majority of instances, of symptoms referable to a focal cerebral hemispheric lesion, with the clinical onset at a variable time after occurrence of the underlying process, and developing with an accumulative and progressively severe course. In most cases of porencephaly the signs are indicative of focal cerebral lesions which correlate well with the symptoms. The clinical picture, in the majority of patients, early in its course, is mild to moderate in degree, so that it does not precipitate adequate study until adolescence or early adulthood. The only symptoms that apparently improve were seizures of various types, which did so after excision of the cysts or upon adequate anticonvulsive therapy. The pathogenic changes which account for the clinically progressive characteristics of this disease remain to be disclosed and explained.—R. W. Naef, M.D., Clinical Features of Porencepaly, *A. M. A. Archives of Neurology and Psychiatry*, August, 1958.

CHEMICAL LABORATORY

The following paper has been authorized for publication by the Chemical Laboratory.
WALTER WOLMAN, PH.D., *Director.*

IDENTIFICATION GUIDE FOR SOLID DOSAGE FORMS

John J. Hefferren, Ph.D., Chicago

The need to identify rapidly an unknown tablet or capsule frequently occurs in a wide variety of circumstances. In such cases, a qualitative chemical analysis followed by confirmation tests frequently is a long and difficult task. The time factor, coupled with the limited quantities of the unknown, makes the identification difficult and often impossible.

Methods to aid in identification have involved direct comparisons of the unknown with pictures of known products[1] or with authentic samples carried on various types of display boards. Such methods may suggest the identity of the unknown or eliminate a few possibilities, and in this way they are of some value in identification work but are necessarily limited in scope.

Development of Identity Guide

As a possible aid in drug dosage identification work occasionally undertaken by the A. M. A. Chemical Laboratory, the feasibility of a preliminary screening method, based solely on the physical characteristics of solid drug dosage forms such as tablets and capsules, was investigated. Examination of a number of commercial tablets and capsules quickly made it evident that there were sufficient differences in the several physical characteristics to suggest reliance on them in an identification or screening procedure. To test these initial observations, 100 products were examined and catalogued according to their physical characteristics.

Since the results were encouraging, the study was then extended to 500 samples. These samples, including both prescription and proprietary drugs, were obtained from the drug files of the Chemical Laboratory, physician's samples, and from a commercial drug store. The samples were not selected according to any use-frequency statistics but on the basis of a representative cross section of the physical characteristics of the tablets and capsules.

From the experience gained in examining these 500 products, a dosage identification guide was developed. This system helps one to identify an unknown by following through a series of categories of physical characteristics, with the consequent elimination of many individual drug preparations and the eventual restriction of remaining possibilities to a relative few.

After completion of this pilot study with the 500 products, the dosage identification guide was discussed in detail with representatives of various agencies and specialty groups concerning the feasibility and need for such a scheme in their particular areas. These included physicians, personnel in emergency receiving rooms, the A. M. A. Committee on Toxicology, toxicologists, pharmacists, and medical examiners and representatives of government agencies, poison control centers, the pharmaceutical industry, and law enforcement agencies.

These conferences indicated that such a suggested guide would prove valuable in a number of areas, provided it were available in suitable form. It is planned to make this information available by publication of a text which would include a short discussion of the dosage identification guide, general information on solid drug dosage forms, a set of color reference chips, and data on the physical characteristics of those products examined.

Solid Dosage Identification System

This dosage identification guide (fig. 1) is constructed to accommodate all the individual tablet and capsule preparations on the market. The guide has three main categories: tablets, soft gelatin capsules, and hard gelatin capsules. In each of these categories is listed a number of terms to describe the individual characteristic under such headings as coating, shape, coloring, contents, markings, scoring, and size.

The shapes of the various tablets and capsules used in the dosage identification guide are illustrated in figure 2. When the tablets are viewed from the side, one of the most characteristic differences between sugar-coated, uncoated, and film-coated tablets is easily seen. Since sugar-coated (pan-coated) tablets are coated by tumbling, all the ridges resulting from compression of the core are rounded by subsequent layers of coating material. Film-coated tablets are coated by dipping; thus, they have a thin film coat but retain ridges characteristic of the uncoated tablet. Some forms of sugar-coated tablets are quite similar to soft

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Chemist, American Medical Association.

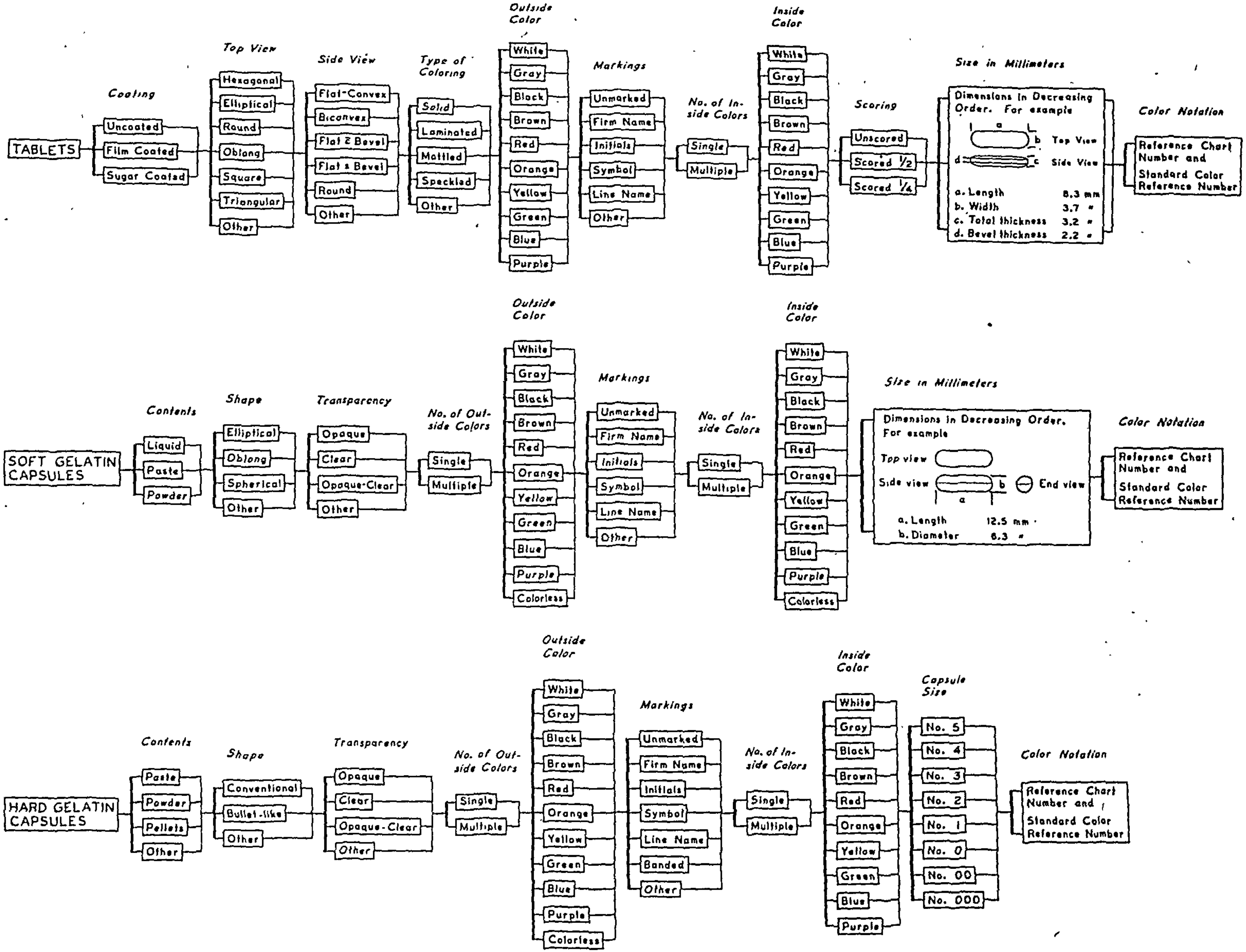


Fig. 1.—Dosage identification guide.

gelatin capsules. The essential differences are that the soft gelatin capsule has a seam at the point of closure of the two halves, and the contents can be liquid, paste, or powder. The sugar-coated tablet will not have a seam and will have a compressed core.

In the dosage identification guide (fig. 1), the outside and inside color categories have 10 terms for tablets and 11 for capsules. The use of a limited number of colors at this point in the guide is to facilitate indexing. At the far right of the guide is provision for a more exact color notation of the product.

A more exact color notation is obtained by comparison of the colors of the product with a set of reference color chips, which will be included with the identification text. For example, a sugar-coated tablet might be described by using the limited color terms as outside color, red, and inside color, brown, whereas in the color notation category, these two colors might be more accurately described in relation to the reference chips as red no. 2 and tan no. 1 respectively.

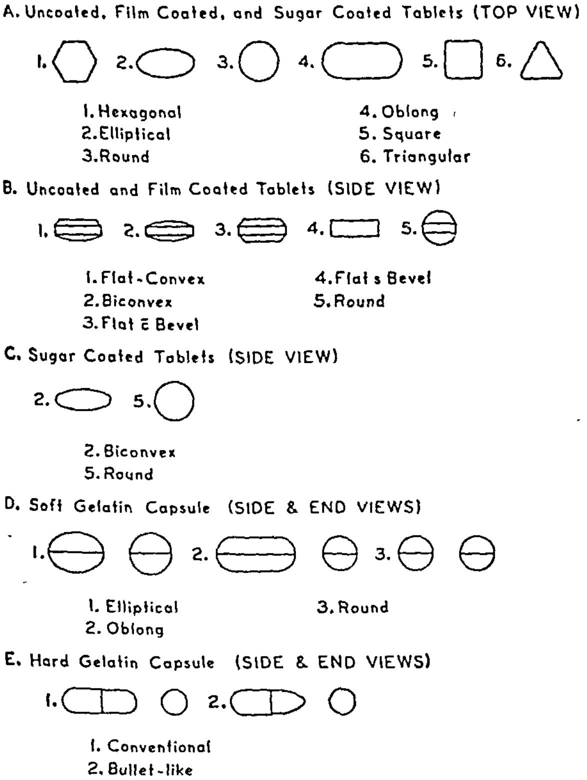


Fig. 2.—Common tablet and capsule shapes.

The color of each product will also be notated by reference to a commercially available color text. This information will be of value only to those who have that text and would constitute an auxiliary refinement of the identification guide. This additional color notation system would not be necessary for the normal use of the system.

The data reported for the dimensions of tablets and capsules are subject to three sources of variation. They are variation due to (1) manufacture, (2) limitations of the measuring device, and (3) precision of the measurements. The magnitude of these sources of variability will be dependent, in part, on the particular type of tablet or capsule.

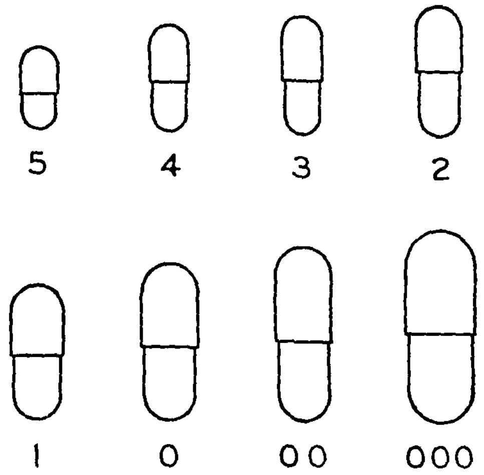


Fig. 3.—Standard capsule sizes (actual size).

Due to its method of manufacture, the size of an uncoated (pressed powder) tablet is most readily reproduced within the same lot and between lots. The diameter of such a tablet is determined by the diameter of the die used in the compression of the tablet and is usually duplicated to within 0.1 mm. On the other hand, the total thickness is a less accurate dimension because of manufacturing variables such as granulation density. The duplication of this dimension, however, is usually within 0.3 mm., depending to some extent on the size of the tablet. The measurement at the bevel edge is

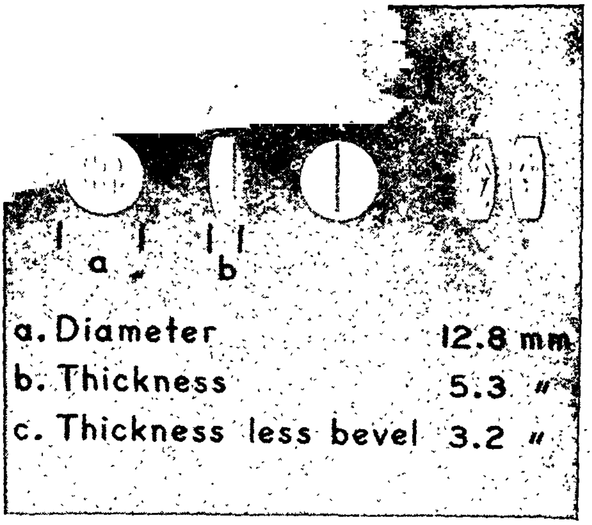
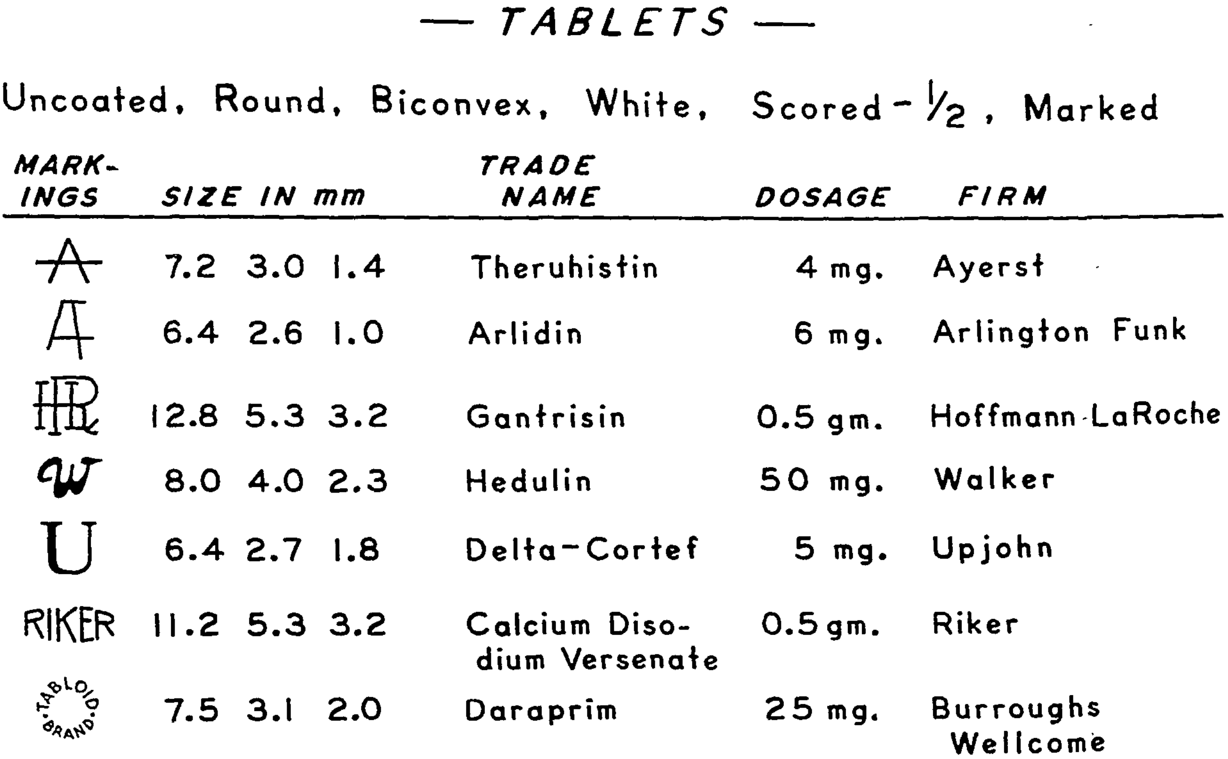


Fig. 4.—Physical characteristics of sample tablet.

related to and has the same variables as that of the total thickness, plus the added variable due to greater difficulty in obtaining as accurate a reading at the edge with a measuring device. With uncoated, pressed powder tablets, the dimensions in decreasing order of reproducibility are diameter, total thickness, and bevel thickness.

With film-coated and sugar-coated tablets and soft gelatin capsules, a wider range of dimensional variability results because of the methods of manufacture. These products (with the exception of film-coated tablets) do not have a bevel measurement and as a result have one less dimension than does the comparable shape in an uncoated tablet. Thus, the dimensions of film-coated and sugar-coated tablets and soft gelatin capsules are somewhat less definitive than are those of an uncoated tablet; however, this is somewhat offset by the many colors and types of contents which these products usually have.



— TABLETS —

Uncoated, Round, Biconvex, White, Scored-½, Marked

MARKINGS	SIZE IN mm			TRADE NAME	DOSAGE	FIRM
	7.2	3.0	1.4	Theruhistin	4 mg.	Ayerst
	6.4	2.6	1.0	Arlidin	6 mg.	Arlington Funk
	12.8	5.3	3.2	Gantrisin	0.5 gm.	Hoffmann-LaRoche
	8.0	4.0	2.3	Hedulin	50 mg.	Walker
U	6.4	2.7	1.8	Delta-Cortef	5 mg.	Upjohn
RIKER	11.2	5.3	3.2	Calcium Disodium Versenate	0.5 gm.	Riker
TABLOID BRAND	7.5	3.1	2.0	Daraprim	25 mg.	Burroughs Wellcome

Fig. 5.—Idealized page of future text on identification of solid dosage forms.

All measurements of tablets and soft gelatin capsules are made with a vernier calipers reading to 0.1 mm. The size of a hard gelatin capsule is determined by comparison to a chart of standard capsule sizes (fig. 3). These capsule sizes are accepted throughout the pharmaceutical industry and represent the most convenient way to describe the size of a hard gelatin capsule.

Application of Dosage Identification Guide

To illustrate the application of the dosage identification guide to a specific problem of identification, the commercially available tablet pictured in figure 4 can be used as an example of an unknown. Using the guide, figure 1, the term best describing this tablet in each category such as coating, top view, etc., is selected. For this tablet, the terms and the corresponding categories of physical classification would be as follows:

Coating	uncoated	No. of inside colors	single
Top view	round	Inside color	white
Side view	biconvex	Scoring	scored-½
Type of coating	solid	Dimensions	12.8, 5.3, 3.2 mm.
Outside color	white	Color notation	white
Markings	initials		

After the selection of those terms best describing the physical characteristics of this tablet, the text containing similarly obtained listings for commercially available tablets and capsules is referred to for the possible solution to the identity of the unknown. An abbreviated and idealized page of this text might look like that shown in figure 5. This page contains a listing of tablets which are uncoated, round, biconvex, white, marked, and scored-½. The third product listed has the same physical characteristics, markings, and dimensions as the tablet in figure 4, so the tablet is probably the 0.5-Gm. tablet of sulfisoxazole (Gantrisin) manufactured by Hoffmann-LaRoche. Positive identification of this tablet should then be made by some confirmatory test.

In figure 6, the application of this guide and text to 500 products demonstrated its workability with a variety of tablets and capsules, ranging from the unusually shaped, well-marked products to the

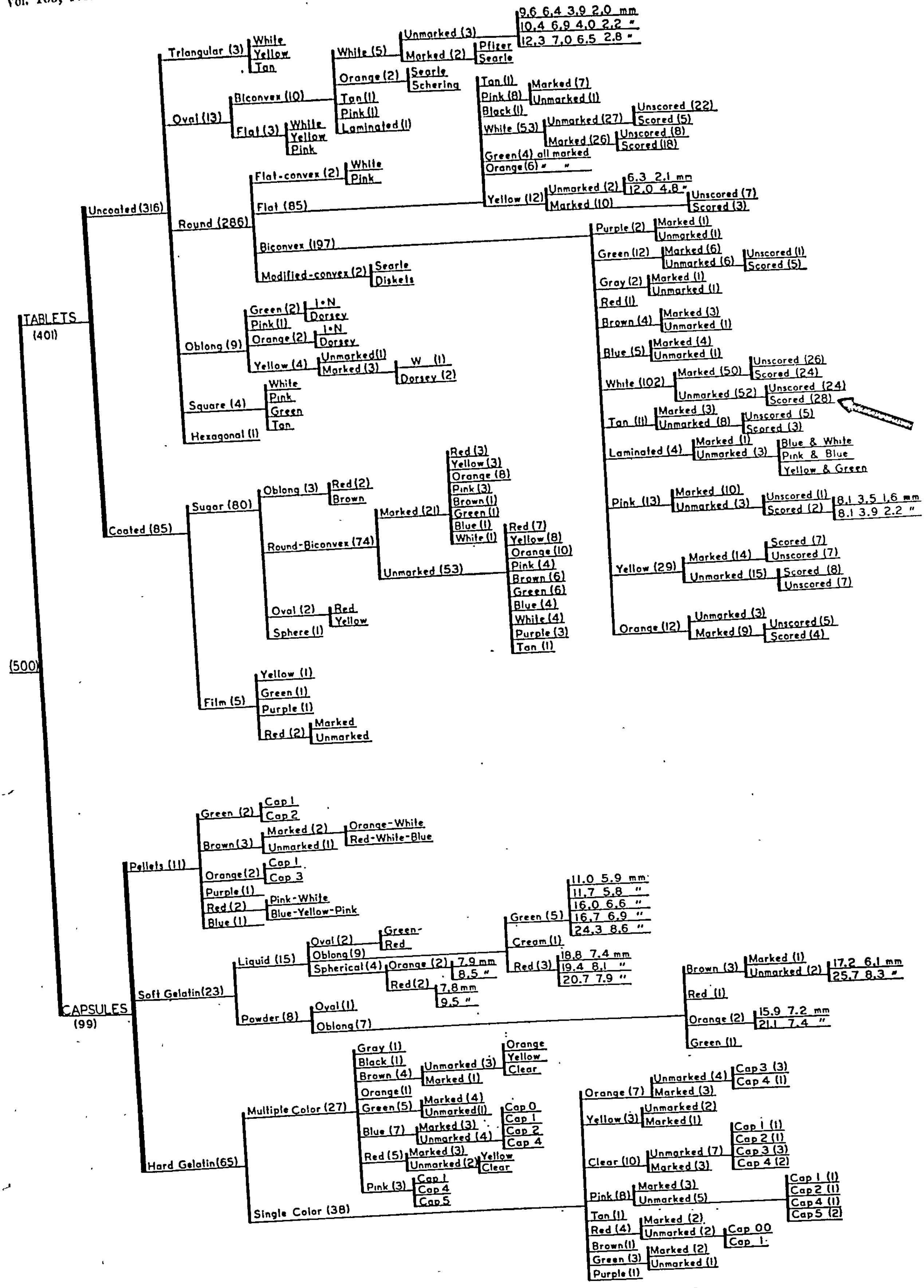
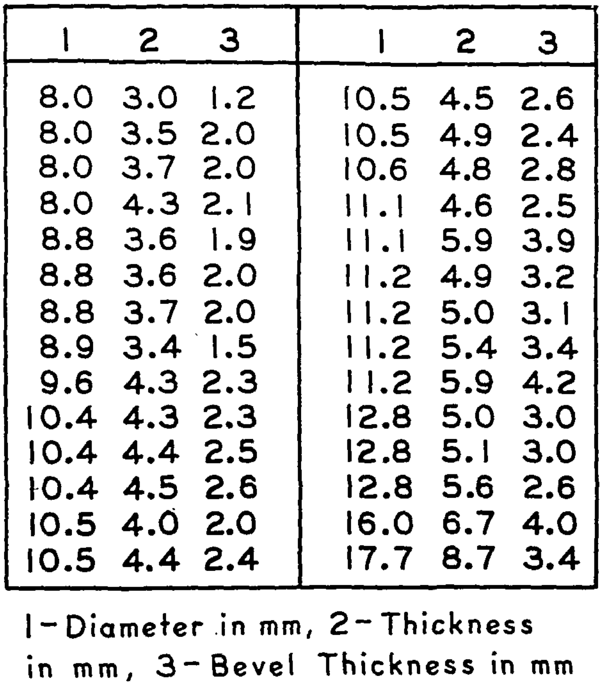


Fig. 6.—Breakdown of 500 products used in pilot study.

familiarly shaped, unmarked products. Proceeding from left to right across the chart, gradual elimination or separation of the 500 products into groups occurs. The numbers in parentheses on the chart represent the number of individual products remaining in that group.

At the far right of the chart, wherever the breakdown ends as marked products, there are still two further aids to identification, that is, the dimensions and the actual markings such as symbols, initials, or names. In these cases complete separation usually occurs, leaving no two products in the group alike in every physical characteristic utilized by the coding system.

On the other hand, the unmarked categories, such as that indicated by the arrow in figure 6, can be further separated only on the basis of size. This tablet group—uncoated, round, biconvex, white, unmarked, and scored-½—contains 28 products, which is the largest group in the sampling of 500 products.



1	2	3	1	2	3
8.0	3.0	1.2	10.5	4.5	2.6
8.0	3.5	2.0	10.5	4.9	2.4
8.0	3.7	2.0	10.6	4.8	2.8
8.0	4.3	2.1	11.1	4.6	2.5
8.8	3.6	1.9	11.1	5.9	3.9
8.8	3.6	2.0	11.2	4.9	3.2
8.8	3.7	2.0	11.2	5.0	3.1
8.9	3.4	1.5	11.2	5.4	3.4
9.6	4.3	2.3	11.2	5.9	4.2
10.4	4.3	2.3	12.8	5.0	3.0
10.4	4.4	2.5	12.8	5.1	3.0
10.4	4.5	2.6	12.8	5.6	2.6
10.5	4.0	2.0	16.0	6.7	4.0
10.5	4.4	2.4	17.7	8.7	3.4

1-Diameter in mm, 2-Thickness in mm, 3-Bevel Thickness in mm

Fig. 7.—Dimensions of uncoated, round, biconvex, white, unmarked, and scored-½ tablets.

The sizes of these 28 products are listed in figure 7. The first 4 of these products have the same diameter of 8.0 mm., whereas the other 24 products are sufficiently different to be eliminated by this first measurement. The thickness of the first and fourth separate them from the second and third products; however, the third measurement fails to achieve any further separation. Reference to the text will indicate what the drug compositions may be. Identification is then relatively simple by application of confirmatory tests for these substances.

There are eight tablets in figure 7 with a diameter between 10.4 mm. and 10.6 mm. Thickness measurements eliminate three of these products (4.0, 4.8, 4.9); thus, the remaining five represent 1% of the 500 products used in this initial study. It is recognized that when thousands of samples instead of 500 are examined and coded into the scheme, the total number of individual products in such a nondistinguishable group will be much greater, even though the percentage of the total may not change.

Present Status

The examination and coding of commercial drug products is under way. A list and samples of those drugs which represent approximately 87% of the prescription drugs used have been obtained and coded. The same approach is being applied to the proprietary drugs. With these most frequently used drugs as a core, coding is extending to other commercially available tablets and capsules.

Extension of the coding system to include other solid drug dosage forms such as suppositories is planned. Some nondrug products such as plant foods, which are now commercially available in tablets and capsules, will also be included.

It is planned that all the data obtained from coding the physical characteristics of these products will be organized and published in text form together with the dosage identification guide, color reference chips, and instructions for use. It is hoped that the first edition of this text including some 5,000 listings will be published in about a year. Thereafter, supplements and new editions will be published to include new products and those old products whose physical characteristics will have been changed. Further editions will be expanded then to include all the commercial drug products obtainable.

The success of this project depends on obtaining authentic drug samples. This is one of the most difficult problems in this work, and it is hoped that samples will be made available to us by the many firms, individuals, and agencies who have such products. At least six individual tablets and capsules of each size, the name of the product and of the manufacturer, and dosage size are essential for coding purposes.

The color reference chips used in the text will be selected and prepared with the assistance and advice of Mr. Carl Foss, Princeton, N. J.

The list representing 87% of prescription drugs used in this study was developed and contributed by Mr. David D. Stiles of Abbott Laboratories, North Chicago, Ill., from a prescription survey project carried out under his direction.

The samples of these prescription drugs were gathered and contributed by Sargent's Drug Stores, Inc., Chicago, through the courtesy of Mr. William Morse.

Reference

1. Tablet and Capsule Identification Guide, 1956, Chemist and Druggist: Annual Special Issue, pp. 603-606, June 30, 1956; Tablet Identification 1958, ibid., pp. 698-703, June 28, 1958.

Cost of Medical Care

As the American's income has risen, so has his annual expenditure for individual health services—only more so. The Health Information Foundation last month reported that, whereas 3.7% of the consumer-expenditure dollar went for health services in 1929, the comparable 1957 figure was 5.3%.

HIF attributes this to two facts: the quantity and variety of private health services and the vastly improved quality. The foundation stated: "Pain, disability, and serious illness could be faced at relatively little expense in the past because there was little that could be done for a sick person. Now pain and disability can often be avoided, and death greatly postponed—but at the cost of more visits to physicians, more admission to hospitals, more use of drugs and other treatments."

Not only has the gross amount spent for these health services increased (to 15 billion dollars in 1957), according to HIF, but the proportionate share spent for insurance, drugs, and hospital and professional services has undergone revision.

The foundation states, for example, that physicians' services took almost 33 cents out of the 1929 medical care dollar, whereas by 1957 this share dropped to less than 25 cents. Conversely, says HIF, hospitals in 1929 were receiving less than 14 cents, but by 1957 were taking almost 26 cents of that dollar.

MEDICINE AT WORK

- *People and Crashes*
- *Ahead in Mental Health*
- *Saving for Medical Bills*
- *Worker Health Survey*
- *The Moon Is 'Old Hat'*
- *Talk with Pioneer Space Doctor*

A. M. A. Committee in discussion of auto safety last month. Left to right are Drs. Horace Campbell, John Rodger, James Goddard, Charles Hayman (guest participant), Jacob Kulowski, and (back to camera) Fletcher Woodward, chairman.

—J. A. M. A. photo

Human Inadequacy—Is It the Vital Clue to Safety on the Highway?

> "Only a mass of crumpled metal that once had been an automobile remained today to offer mute testimony to the speed with which a salesman's car struck a freight train last night. . . . ." (Illinois)
>
> "Four teen agers died today as the car in which they were riding ran head on into a semi-trailer truck on a mountain road . . . " (Colorado)
>
> "Seven lost their lives and two more were injured yesterday in a collision that resulted when two cars, traveling in opposite directions, attempted simultaneously to pass the vehicles in front of them on a three-lane highway. . . . ." (Indiana)

News stories such as these daily record the terrible toll of highway tragedy that has become an almost accepted part of the American scene. Night or day, main highway or back road, kids in their teens or a pair of grandparents—day after day the slaughter has continued virtually unchecked to reach an estimated total last year of 37,000 dead; another one and one-third million with disabling injuries. The motor vehicle, which as much as any single invention brought Americans to their peak of material comfort, has also brought a record of death and crippling injury so staggering that one writer even pointed out its efficacy as a method of population control.

One group that two years ago sank its teeth into the accident problem was the A. M. A.'s Special Committee on Medical Aspects of Automobile Injuries and Deaths (see Medicine at Work, THE JOURNAL, Oct. 27, 1956). Its Chairman, Dr. Fletcher Woodward of Charlottesville, Va., reduced the problem to its essentials when he wrote: "The highway traffic accident problem has three main components—the driver, the highway, and the vehicle. Today, human failure overshadows all other factors in the production of highway accidents."

Guides to Driving Ability

Starting with this basic assumption, the Committee has spent its first two years in the production of three guides. One-half million copies of the Committee's 15-page booklet, "Are You Fit to Drive?" have been made available to the public through physicians and insurance companies. Colorfully illustrated, it outlines a series of conditions that affect individual capacity to operate a motor vehicle. More explicit and comprehensive is the soon-to-be-published "Medical Guide for Physicians in Determining Fitness to Drive a Motor Vehicle" which received a final polish when the Committee met in Chicago last month.

Both publications deal—as will the forthcoming "Medical Guide for

A bumper-triggered, hydraulic system that pulls the driver's seat forward and tilts it to the rear with a scooping motion in 0.0031 of a second is being offered as a possible antidote to front-end collision injuries. The device allows front-seat passengers to take impact force on their hindquarters. The system, manufactured by Protect-O-Matic Corp., was demonstrated in an action film on test crashes (*right*) shown last month to the A. M. A. Committee on Medical Aspects of Automobile Injuries and Deaths. Test drivers have emerged uninjured in 50-mph collisions, the manufacturer claims.

Licensing Authorities"—with physical, emotional, and toxicological states that affect individual competence behind the wheel. The "Medical Guide for Physicians" states: "The physician is the person best able to ascertain the physical, mental, emotional, or physiological impairments of an individual. Moreover, he is in a good position to evaluate these impairments in relation to safe driving ability."

How much of a role does the physical and mental condition of a driver play in highway accidents? Nobody knows for sure, but there have been some informed guesses. Capt. R. C. Blossom, research and development officer of the California Highway Patrol, offered one last summer when he spoke at the A. M. A.'s Annual Meeting in San Francisco. He said: "An analysis of coroners' reports covering 653 motor vehicle deaths indicates 62 may have been due to natural causes. From this small sample, plus logic, it would appear that existing and induced physiological conditions of drivers involved in fatal auto accidents may constitute a major portion of the true causes of death in an automobile."

With its three guides, the Committee hopes in time to be able to discourage persons with potential disabilities from operating motor vehicles. In addition, members of the Committee have written, and in some cases testified before legislative bodies, of the value of safety design in motor cars, the need for seat belts, and the dangerous impact of even limited alcohol usage on driving ability.

Others Work for Safety

Other new and continuing efforts include:

—The A. M. A. joined with the National Safety Council and the Public Health Service last month to revive flagging interest in the injury-reducing potential of seat belts for passenger cars.

—A 14-man team from the Department of Legal Medicine of the Harvard Medical School this month began a five-year study of fatal auto accidents supported by an $809,000 federal grant. Efforts will be made to trace the erring motorist's physical and psychological history to determine factors that may have affected his driving ability.

These efforts all have one thing in common. They recognize the responsibility of the individual motor vehicle operator as the prime causative factor in accidents. Dr. Harry H. Wagenheim, director of psychosomatic service at Temple University Medical Center, pinpointed this responsibility when he said: "Automobiles don't kill people. Drivers kill people."

Dr. Fletcher D. Woodward of Charlottesville, Va., is Chairman of the A. M. A. Committee on Medical Aspects of Automobile Injuries and Deaths. Vice-chairman is Horace E. Campbell of Denver. Other members are Drs. Jacob Kulowski of St. Joseph, Mo.; Harold M. Brandaleone of New York City; John R. Rodger of Bellaire, Mich.; Seward E. Miller of Ann Arbor, Mich.; James L. Goddard of Washington, D. C.; and Ross McFarland, Ph.D., of Boston. Staff Secretary is Mr. Howard Schulz.

What's Ahead in Mental Health? Conference Is Sounding Board

Can medicine cope with the communicability of certain mental and emotional disorders? What are some of the problems of "learning deficits" in children? Why do mental illness and health in aged persons present a special challenge to medicine? How can physicians and medical students best be trained in psychiatric medicine? What are some problems of the Joint Commission on Mental Illness and Health, and how has it progressed?

Those five broad questions were tackled several weeks ago in separate round-table discussions by 140 representatives of 42 state medical associations and seven national health organizations.[*] Transcripts of the Fifth Annual Conference sponsored by the American Medical Association and its Council on Mental Health last Nov. 21 and 22 in Chicago now are being compiled. At a banquet in mid-session, both A. M. A. President Gunnar Gundersen and Dr. Jonas Salk pointed out the similarity of certain aspects of physical and mental disorders.

Dr. Salk, who is professor of experimental medicine and director of the Virus Research Laboratory at the University of Pittsburgh, cited analogies between the personal immunity to physical disease and that developed against mental illness. Dr. Gundersen told the participants: "Tuberculosis, along with many other diseases, is not related to a single causative agent. It, as well as mental and emotional illness, seems to be multifactorial in the sense that social factors enter into the causation of both." Earlier, Dr. Salk said:

> The idea of communicability of mental and emotional illness requires now a recasting of the concept of causation, etiologic factors, and pathogenesis. A fresh examination from the purely biological viewpoint would be most helpful. Is not the plasticity of the individual during his developmental period the heart of the matter? When the individual has got beyond a certain point in development, he no longer is susceptible to this particular malady, but he may be susceptible to another, whether it is Orson Welles fantasy or something that happens on television for a child audience. The individual is still growing, still changing. All that he is, is not determined by his genes but by a number of events that occur after birth. Why cannot we visualize this as a dynamic situation where there are different degrees of sensitivity or susceptibility or sensibility to different stimuli or different events at different points from the moment of conception to the moment of death?

Following are other summary excerpts from the conference:

Problems of Learning Deficits in Children.—"Isolationism is a relatively uncommon situation, but frequent enough to demand of the physician that he look into absolute rejection by parents. On file is the interesting case of isolationism in a child who had an IQ of 52 at the hospital where he was studied, and with good care and training he showed two years of mental growth in three months. Frequently parents get the feeling that their child is not developing normally, mentally. They do not know where to get help. There are as yet many untrained people in the field. There are not enough psychiatrists in the general population, and only about 200 child psychiatrists who are qualified in the U. S. As a result the burden is placed on the general practitioner. Most often the teacher is the first to find the difficulty but there is a danger that by the time the child who has a mental deficit gets into school the damage might be irreversible. . . . Reading deficits need a great deal of study. Much is known today about reading disabilities and it is tragic when the child who has a reading disability is diagnosed as mentally retarded. . . . Schools for retarded children should not be for adults. There is need for separation of delinquent and aggressive defectives from the child who can be trained."

Education for Psychiatric Medicine.—"Preceptorship training is, by far, the best way to teach psychiatric principles. . . . Medical students seem to learn the didactic or scientific aspects of psychiatry while retaining their cultural prejudices. Influencing such a student with good psychiatric principles could begin at the grade school level and become increasingly important in his premedical education. It is difficult to describe the kind of person who would do best in psychiatry or utilize psychiatric principles in the general practice of medicine. The most common phrase to describe him is that he 'must like people.' . . . What makes a good physician has not been well conceptualized. Admission committees seem to select students on the basis of whether they will pass in medical school and not on the basis of whether they will be good physicians."

Progress and Problems of the Joint Commission on Mental Illness and Health.—The effects of iproniazid and electroshock were discussed as examples of areas of study that should be undertaken. "The Joint Commission should plan projects that are concerned with research in relation to patients' care and what happens to patients after

Dr. Leo H. Bartemeier of Baltimore is Chairman of the A. M. A. Council on Mental Health. Other members are Drs. Lauren H. Smith of Philadelphia, Vice-chairman; Walter H. Baer of Peoria, Ill.; Norman Q. Brill of Los Angeles; Hugh T. Carmichael of Chicago; Hamilton Ford of Galveston, Tex.; Francis M. Forster of Madison, Wis.; George E. Gardner of Boston; and M. Ralph Kaufman of New York City. Dr. Richard J. Plunkett is Staff Secretary.

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[*] The American Hospital Association, American Medical Association, American Psychiatric Association, American Psychoanalytic Association, Council of State Governments, Joint Commission on Mental Illness and Health, and National Committee Against Mental Illness.

psychotherapy. If the Commission is to be extended, more psychiatrically trained doctors should be obtained." There was much discussion of the idea of practicing psychiatrists' engaging in projects within the area of their practice, pooling their information two or three times a year, and then making their reports to the Joint Commission.

(The Joint Commission on Mental Illness and Health is a research and educational organization founded in 1955 by the American Psychiatric Association and the A. M. A. with the cooperation of several dozen other groups to study resources available for the detection, treatment, and rehabilitation of the mentally ill.)

Mental Illness and Health in the Aged.—"We cannot at this time elaborate the problems of housing and the senior citizen, or the economic factors that include insurance and pension plans. Often the economic factors are secondary to emotional needs. There is need to consider whether social values can be changed to make old age an honorable state. Too much premium has been placed on the cult of youth and beauty. There is need to encourage children to feel a sense of responsibility toward aging parents. . . . There is considerable clinical evidence to show that good medical treatment can get 25% of the mental hospital patients over the age of 65 back into the community, and as high as 70% of depressions of old age sufficiently relieved so that they can resume normal living. . . . Whenever possible, the old person should be maintained in his own home. . . . An active and productive life is a protection against emotional decomposition in old age."

Communicability

The conference participants gave special attention—both in a separate round table session and in general discussion—to the relatively unexplored concept of the communicability of mental and emotional illness and health. A summary report stated:

> This concept was a relatively new and provocative one which stimulated a wide variety of thinking within the group, ranging from a description of outstanding examples of "epidemics" of emotional disturbance—such as the panic resulting from Orson Welles' radio broadcast [in 1938, depicting realistically in news format an attack by invaders from another planet], panty raids in colleges, and certain types of religious revivals clearly related to environmental factors—to individual personal experiences with emotional disturbance arising out of distorted thoughts, feelings, and attitudes transmitted between family members. The concept of communicability of mental health is a concept of equal importance with that of communicability of mental disorder.

As participants warmed to the subject, they voiced provocative ideas such as the following:

"It seems a substantial number of patients become mentally disturbed by talks with their doctors."

"The kind of communicability that exists in mental illness is much greater than in measles or other similar diseases."

"In the field of neuroses, anxiety-ridden parents or teachers may evoke anxiety reactions in their children or pupils. Poor leadership with subsequent defective morals prepares the groundwork for a

Selected Quotes from A.M.A.'s Annual Mental Health Conference

ON OLD PEOPLE—

Many of the people who reach old age become a problem because they are isolates. They have no families on whom they can rely. . . . Family relationships frequently are stressful, and some of the problems of old age are the expressions of some of that stress. —Discussion on "Mental Illness and Health in the Aged."

Too often when we follow the urge to rid ourselves of a burden like old people, we send them to a hospital. And I tell you, when that happens, the old life is shortened. Maybe we as physicians should stand up and not too easily agree with families that want to hospitalize their elders.

—Dr. Leo H. Bartemeier, Chairman, Council on Mental Health.

ON CHILDREN—

The more that psychiatrists can contribute to the diagnostic field, the greater chances there will be that many children who are presently diagnosed as feeble-minded, mentally-retarded, etc., will not fall into this category. . . . Many are not in this category at all.

—Discussion on "The Problems of Learning Deficits in Children."

ON COMMUNICATING THE ILLNESS—

The concept of the communicability of mental disorder should be accorded all possible consideration in research planning. . . . Efforts directed toward training psychiatrists in this important field should be commended. . . . Psychiatrists do not now generally have the epidemiological orientation required for the development of a conceptual framework for epidemiological study of mental disorder.

—Discussion on "Communicability of Mental and Emotional Illness."

In years past, nostalgically speaking, the public health and epidemiological approach to specific disease high incidence of emotional illness which is communicated."

"Since the word 'communicability' has had a specific medical sense for centuries, are we justified in giving this word an enlarged meaning? It would be ridiculous to try to defend the assertion that all mental disorders are communicable."

"The epidemiology of healthy ideas and healthy behavior is an epidemiology of the future."

"I suspect there is a very direct correlation between the general level of emotional maturity in individual members of a given culture and the decline of that culture. What are the socioeconomic and governmental factors which prevent the maturation capability in our citizens? Medicine as a whole should spend a lot of time thinking about this and talking about it. This is an excellent opportunity for organized medicine to get together with the sociologists, the historians, the law enforcement representatives, and others—to lead our country's cultural development instead of following it. Educators are as alarmed as we physicians are at the 'cultural deterioration,' the need for improvement."

"During the Hitler regime paranoia became not merely an epidemic, but a national policy by one man, against whom large masses of population apparently were unable to immunize themselves."

"In epidemiology, mental disorder has got to develop on a conceptual framework of psychiatry. General epidemiologists can contribute method, but it will never be epidemiology of mental disorders unless you get psychiatrists who are trained in epidemiological methods, and that is one of the critical things we need."

Does She Drive Him to Drink? Plan Aids to Wives of Alcoholics

"The wife is often a critical link in the rehabilitation of an alcoholic husband. She can help him, or she may, without intent, almost literally drive him to drink." Based on this theory, the Chicago Committee on Alcoholism this month announced plans for new group and individual services for wives.

The committee recently spent several months offering such services on an experimental basis, and the experiment was considered successful.

Dr. Patrick Israel, psychiatrist and phychiatric director of the committee, said sessions will be held periodically for wives who feel that their husbands have an alcoholism problem. He said: "They will be given information about the illness of alcoholism and suggestions as to the kind of behavior on the part of the wife which is likely to be most helpful for living with the problem and in getting the husband to understand his own need for obtaining assistance in overcoming his alcoholic pattern."

The committee, which operates Portal House, an outpatient clinic for the treatment of alcoholics, is concerned with education, research, and treatment in the field of alcoholism (see Medicine at Work, The Journal, July 19, 1958).

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problems now would seem to have been fantastically simple, compared to our present problems in mental illness. . . . We face in essence a heretofore unrecognized epidemic throughout our country and the world.

—Dr. Gunnar Gundersen, President of the A.M.A.

The cells that produce polio are conditioned to respond when a virus threatens the body. . . . There is no reason to believe that cells of the nervous system will not respond in the same way as cells that create the immunity to polio. We are really concerned with the problem of biology as it relates to many fields.

—Dr. Jonas Salk, University of Pittsburgh School of Medicine.

ON COMMUNICATING THE PROBLEM—

We psychiatrists are not always effectively communicating with our colleagues in medicine. Not enough of us are leaving our ivory towers. No wonder some physicians refer patients to psychologists—instead of to psychiatrists—for psychotherapy. They don't know the differences between psychologists, psychiatrists and psychoanalysts. Because they don't know, they fear—and because they fear, they tend to fight the good that we, who also are in medicine, are trying to do.

—Dr. Alfred Auerback, San Francisco psychiatrist.

Mental health committees [of medical societies] can help educate the governing bodies and the officers of their state medical associations. Furthermore, they can be a great deal of help in education, often by meeting with prominent non-physicians in the state.

—Discussion on "Education for Psychiatric Medicine."

ON INTERNATIONAL COMPARISONS—

The Joint Commission on Mental Illness and Health should make comparative studies between the United States and other countries with regard to methods, procedures and research on various projects. . . . Various countries of the world have different standards of procedure and definition in evaluating mental illness and health.

—Discussion on "The Joint Commission—Progress and Problems."

Survey of Small Plant Occupational Health Programs

Hundreds of small business firms have success stories to tell about their occupational health programs, and the A. M. A. wants to relay those stories to physicians everywhere. To do this, a survey of the various types of medical services provided by physicians in charge of such programs will be made this year by a committee of the Councils on Medical Service and Industrial Health.

The survey will also seek to determine the various arrangements through which these services are provided in the plants employing 500 and fewer workers. Case studies for each program will cover such points as location of establishment, type of industry, types of medical service provided, arrangements and administrative procedures used, origin and objectives of the program, hours of service provided, description of the occupational environment, and relationships between the physician serving the program and other physicians in the community.

Physicians in individual private practice, in clinics, or in various other arrangements through which occupational health services are provided to small plants who would like to take part in the study are invited to communicate with the Committee on Medical Care for Industrial Workers, 535 N. Dearborn St., Chicago 10, for additional details. The committee believes that publication of the case studies will help other physicians and management who are interested in developing such programs where they do not now exist or in evaluating those programs presently in operation.

Can Discoveries Be Coaxed?

Names prominent in pharmacology, research, biochemistry, medical journalism, clinical science, and industrial technology figured on the program of the world's first serendipity ("happy accident") conference which ended two weeks of session today at Nassau, Bahamas.

As "animateurs," they stimulated free discussion among representatives from various disciplines on the role of serendipity (see Medicine at Work, THE JOURNAL, Dec. 21, 1958) in such fields as chemical synthesis, endocrinology, organic disease, enzymology, and neurology. Dr. B. L. Frank of Montreal, who organized this First Bahamas Serendipity Conference, said:

"From the start, our goal has been to break down the barriers between specialized fields and to encourage the cross-fertilization of ideas which might lead to unforeseen results. Perhaps, this way, serendipity can be controlled to the point of coaxing discoveries or inventions—finding something accidentally on purpose."

Each discussion lasted two hours for all participants. Smaller and more informal groups then carried the theme further. Among "animateurs" on the conference program were:

Dr. R. Keith Cannan, chairman, division of medical sciences, National Academy of Sciences.

Dr. Alfred Gilman, professor of pharmacology, Albert Einstein College of Medicine.

Dr. Henry B. Hass, president, Sugar Research Foundation.

Dr. Edward C. Kendall, award-winning biochemist, Princeton University.

Dr. I. Arthur Mirsky, professor of clinical science, University of Pittsburgh School of Medicine.

Bernard E. Schaar, president, Schaar and Company, scientific apparatus.

Dr. Abraham White, associate dean and professor of biochemistry, Albert Einstein College of Medicine.

Dr. Walter F. Riker, professor of pharmacology, Cornell University Medical College.

Dr. Austin E. Smith, former editor, THE JOURNAL.

Tax Deferred Savings—One Way To Pay for Medical Care in Old Age?

If Poor Richard never said "Save for your old age," it's probably only because he didn't think of it. It's the kind of eye-to-the-future thrift that appealed to him.

To encourage just this kind of thriftiness, Frank Dickinson, Ph.D., last month advocated federal legislation allowing workers to salt away up to $100 per year, tax deferred, to pay exclusively for medical needs in old age.

His suggestion came, coincidentally, just as the National Association of Insurance Commissioners approved a change—the first in 17 years—in the mortality table, a statistical record of the rates of death at different ages. "Life expectancy," they said, "has reflected an explosive increase."

Dickinson, who recently retired as head of the A. M. A.'s Bureau of Economic Research, offered his idea Dec. 28 in a paper presented at the American Association of University Teachers of Insurance meeting in Chicago.

Under this plan, any worker would be allowed to put aside up to $100 a year in a special private account. His taxable income for that year would then be reduced by the amount of the deposit. On retirement, the accumulated savings in the special account could be used to meet medical and hospital bills, purchase health insurance, or buy a medical and hospital care annuity. Payment of tax on the money would be made as it was withdrawn.

General Practice and Worker Health

Although the annual Congress on Industrial Health in Cincinnati next month is expected to attract chiefly industrial doctors, it should be of interest to other physicians, too. This is because general practitioners are the ones who provide occupational services for most workers; three-fourths of the nation's labor force is employed in firms not having industrial physicians (see Medicine at Work, The Journal, March 30, 1957).

The Congress, sponsored by the A. M. A. Council on Industrial Health, will be held Feb. 16 through 18 in the Netherland-Hilton Hotel. To be included are:

–A panel discussion of industrial health education at all levels.

–Papers on such research problems as noise, radiation, cancer, and toxicology.

–Reports on cases of industrial disease presented by fellows and staff of the University of Cincinnati Institute of Industrial Health.

Another A. M. A. Meeting Soon

Kansas will be the scene of the 14th National Conference on Rural Health to be held in Wichita March 5 through 7. "Horizons in Rural Health" is the theme of the meeting sponsored by the A. M. A. Council on Rural Health, together with state medical societies and farm, educational, and allied organizations.

Spread 'Homemaker' Idea

Where does a family go for aid when the mother is hospitalized or incapacitated, the father must work, and there are no relatives to help out? In 150 U. S. counties, the obvious answer is "to a homemaker service."

To increase the number of counties in which such an answer is possible is one of the main objectives of the National Conference on Homemaker Services to be held Feb. 10-11 at the Edgewater Beach Hotel in Chicago. Sponsors, in addition to the A. M. A., include 25 voluntary and governmental organizations.

Preconference study groups have prepared 12 working papers which will form the basis for conference talks. One development to be discussed is the sponsorship of a homemaker service by the Passaic County (N. J.) Medical Society and its Woman's Auxiliary.

Information on registration for the conference may be had by writing to the Council on Medical Service, American Medical Association, 535 N. Dearborn St., Chicago 10.

Big City Experiment for AMEF

A five-minute period at the beginning of all departmental meetings held in Minneapolis hospitals in November was used to promote contributions to the American Medical Education Foundation.

Dr. Harold G. Benjamin, AMEF chairman for the Hennepin County Medical Society, said the method was an experiment in solving a major solicitation problem: complete coverage of a large city's physician population. This month the medical society pronounced the experiment a success.

The Moon Is Old Hat

Medicine, Other Sciences Explore Space Frontier

Milton Golin

The Time: Veterans Day, Nov. 11, 1958.

The Occasion: Second International Symposium on the Physics and Medicine of Atmosphere and Space.

The Participants: Hundreds of physicians and other scientists interested in the problems of space conquest.

The Place: San Antonio, the Hilton Hotel–near the scenes of other conquests 112 years ago, when Texans fought the early battles which led to U. S. acquisition of the entire territory west of the Mississippi.

That was the setting near the hallowed bones of Crockett, Bowie, and Travis–pioneers in their own right. But how different were the pioneers of 1958 as they looked toward the decades ahead!

–Sipping soft drinks, they cast unsmiling, sophisticated glances at the lobby sign which read: "Make your next symposium at the Lunar Hilton–1960."

–Elbowing their way through the jammed auditorium doorway as loudspeakers carried program remarks to the adjoining foyer, some of them muttered about lack of space at the space symposium. (The Air Force and the Southwest Research Institute had figured on only 500 participants and a handful of newsmen when they planned the meeting. Nearly 800 showed up, including 73 reporters.)

–Seated comfortably inside, others were regarding moon-region flights as "old hat." Their thoughts were beyond–as they listened to papers on speed-of-light propulsion, closed ecologic systems, problems of rescue in space, the physical environment of Mars.

The forward tone was sounded by James A. Van Allen, Ph.D., head of the department of Physics at the State University of Iowa, when he said: "We would like to emphasize interplanetary or space probes rather than merely moon shoots." Another physicist said: "We have cracked the scientific problem for orbital or lunar flight. It is up to the technologists to follow through. We are concentrating realistically now on probing Mars and Venus."

But what about the medical problems–how close are they to solution? A good many physicians, some of them active in keeping the American Medical Association up to date on such matters, assembled around the time of the symposium to absorb a sort of postgraduate refresher course. They included Dr. Jan Tillisch, Chairman of the A. M. A. Committee on Aviation Medicine which met on the eve of the symposium; Dr. B. Dixon Holland, Staff Secretary of the Committee and its parent Council on Industrial Health; Navy Capt. Oran W. Chennault, M.D., another Committee member; Dr. William J. Kennard, then acting director of the A. M. A. Washington office and an aviation medicine pioneer in his own right; Dr. Richard Meiling, a member of A. M. A. Board of Trustees ad hoc committee concerned with aeronautics and space; Dr. Harold Lueth and Mr. Frank W. Barton, another member and Staff Secretary, respectively, of the ad hoc committee; Dr. Carroll P. Hungate, a member of the A. M. A., Council on National Defense; and the Associate Editor of THE JOURNAL.

A physician even more closely concerned with the health aspects of space flight, Major Gen. Otis O. Benson Jr., commandant of the School of Aviation Medicine at Randolph Air Force Base near San Antonio, told the symposium: "The fact that we have to deal with a multitude of environmental factors shows, more than ever before in the history of human progress, a very close cooperation between physics and engineering on the one hand, and medicine and biology on the other."

Progress of Decade

Next month (on Feb. 9) the School of Aviation Medicine will observe the 10th anniversary of the founding of its space medicine department. Much has happened in the decade since a physician, an astrophysicist, and a bioclimatologist launched operations of the department (see Medicine at Work, THE JOURNAL, June 15, 1957). "Space medicine is a logical extension, is an approved and accredited specialty ranking with the time-honored divisions of medicine," said General Benson. "Now the School of Aviation Medicine has on its staff scientists trained in medicine, space medicine, biology, botany, psychology, biometrics, mathematics, electronics, biophysics, radiobiology, microbiology, astrophysics, and engineering. We also have a number of skilled pilots, many who have scientific training."

One such man is designer-engineer-test pilot A. Scott Crossfield of North American Aviation, Inc., who spoke at the symposium. This month, in a rocket-powered X-15, he was scheduled to be the first man to fly an airplane designed to journey weightlessly (for him) into space 100 miles or more above earth. He said: "Aeromedical problems in orbit are—in order of importance—boredom, zero g [weightlessness], radiation, and then some of the difficulties of detachment. The boredom thing is serious. It is nature that a pilot literally goes to sleep at the switch when he has nothing to do. Demanding tasks enhance his entire performance."

Following are other medically oriented comments from symposium participants:

ON WEIGHTLESSNESS—

There is now a statistically, significantly founded basis for the assumption that man can handle the zero gravity situation for short periods of time. The final answer concerning longer periods, however, can only be found in a manned orbiting vehicle. It is up to the ingenuity of the engineer to invent magnetic and other kinds of devices which may provide a make-believe gravity.

—Hubertus Strughold, M.D., professor of space medicine (see interview in this section of THE JOURNAL).

We are concerned that when the weightless state becomes longer there may develop minor physiologic disturbances which, if cumulative or irritating, may cause or enhance psychiatric symptoms. We can best investigate this by utilizing our rocket capabilities to establish biological laboratories in the sky.

—Siegfried J. Gerathewohl, Ph.D., research psychologist for Army Ballistics Missile Agency.

ON RADIATION—

The cosmic ray measurements of our space satellites and probes have brought about a revolutionary change in the basic concept of the extra-atmospheric radiation field. . . . A radiation intensity prevails which would administer a lethal dosage in a few hours' exposure.

—Herman J. Schaefer, Ph.D., research scientist in radiation biophysics at U. S. Naval School of Aviation Medicine.

ON DETACHMENT—

Exposure to "everyday life" in space over a period of one to several weeks, or even months, in an orbital test bed is an important factor in conditioning a space crew for prolonged absence from earth.

—Krafft A. Ehricke, assistant to the chief engineer at Convair-Astronautics.

ON STRESS—

Studies at this time indicate that man is adaptable, enduring and strong enough to withstand the stresses anticipated, and through the use of sealed cabins, he can be indoctrinated and trained to acceptable performance levels.

—Lieut. Col. George R. Steinkamp, chief of the Department of Astroecology at Air Force School of Aviation Medicine.

ON NUTRITION—

The yeast cycle is being considered to provide a method for stabilizing human waste products by means of bacteria and to make the waste available as appropriate food for both algae and the yeast. Whether a large quantity of yeast could be eaten to operate this cycle over long periods is not known. . . . The interposition of an animal such as a goat, a daphnia, a slug, a snail, or some other animal which is likely to eat algae directly would yield animal protein for the space crew.

—Robert G. Tischer, Ph.D., head of the Department of Bacteriology at Mississippi State University.

During a weightless state, a certain danger exists when attempting to drink from an open container. The liquid tends to disperse upon contact with the lips, and to slip into the sinuses and the respiratory tract. The danger of aspiration is real. Sucking or squeezing the liquid from a bottle solves this problem.

—Siegfried J. Gerathewohl.

ON HEALTH HAZARDS GENERALLY—

Man has not had to cope with the following unknowns he will encounter during our initial space flights: Extended periods of weightlessness, extended periods of isolation

AIR WOR

> and/or confinement, eating and sleeping and working and accomplishing normal body functions under hostile environmental conditions, high accelerations and decelerations, high temperature, low pressure and radiation. . . . And yet, these problems are not insurmountable. A capsule can be built within the weight limitations of our available propulsive capability, thus allowing us to achieve manned space flight soon.
>
> —Major Gen. Bernard A. Schreiver, commander of the Ballistics Missile Division, Air Research and Development Command.

How soon will the U. S. achieve manned space flight? Sooner than many people believe, according to the journal, *Missiles and Rockets.* It reports that a joint military-industry program—complete with formal specifications—is now under way for construction of a 2,000-pound manned satellite capsule that would replace the nose cone of a standard Atlas intercontinental missile to be launched from Cape Canaveral, Fla. Several dozen contractors were supposed to submit bids on the project last month, with trial launchings (first with dummy payloads and then with small animals) expected soon after construction begins this year. Already, the Air Force is laying plans to send a number of two-pound monkeys separately into orbit by the middle of this year, according to Brig. Gen. Donald D. Flickinger, director of life sciences for the Air Research and Development Command.

Words, Actions, Trends

Those are the words, actions, and plans which portray the rocketing rise of space medicine as physicians join with other scientists in an upward-look-with-feet-on-ground. There will be more space medicine symposiums—like the one at San Antonio—and at the regional level, too, like the ones sponsored by medical educators in Santa Monica, Calif., last Oct. 22, by the Bexar County Medical Society in Texas the same month, and by the San Mateo County (Calif.) Medical Society last September.

There will be greater interest at top federal levels, as policymakers—selecting a civil air surgeon—consider his qualifications to attack both physiological and psychological problems involving high-speed jet and rocket flight. And there will be world-wide concern, too, as 15 nations (including the U. S. and the U. S. S. R.) assign nonpolitical representatives to the new international committee to coordinate space research (COSPAR) later this year.

The race for space supremacy is so intense, and yet so broadly attractive, that even amid tight secrecy within individual nations, statesmen call for letting down the bars. One side of that paradox is personified by the FBI agents who kept a constant watch on an uninvited Polish biologist who had "crashed" the symposium at San Antonio. The other side is heard in the words of U. S. Senator Lyndon Johnson at the same meeting: "In a world circled by vehicles of space, there can be no secrets. We need, therefore, to concern ourselves not with guarding what we know but, rather, with exchanging and pooling our knowledge with all the community of free men. . . . The space frontier is, above all, a perpetual frontier."

Medicine has become a partner with other sciences in the exploration of that frontier—and the profession may expect research rewards that can benefit the man on the ground as well as the man in outer space. The former Air Force surgeon general, Dan Ogle, has pointed out that techniques in miniaturizing and otherwise refining instruments for recording animal reactions aloft is hastening the improvement of many professional appliances in terrestrial diagnostic procedures for humans. He says: "Maybe these new devices will help save the life of an Ozark woman whose hill doctor was stumped."

General Flickinger believes that the study of mice catapulted into radiation zones may one day furnish leads for cancer research. Other physicians foresee a variety of untold benefits accruing from space findings directly to earth application. Dr. Hubertus Strughold expresses the point this way:

"The extension of medical research into the extraterrestrial realm of space will not only promote man's conquest of space, it will also broaden our knowledge in medicine and biology in general and, therefore, will be of general benefit to mankind."

Three scientists chat informally at symposium on space medicine and physics in San Antonio. *Left to right,* Wernher Von Braun, Ph.D., technical director of the Army Ballistic Missile Agency at Huntsville, Ala.; Hubertus Strughold, M.D., professor of space medicine at Randolph Air Force Base, Texas; and L. R. Shepherd, Ph.D., chairman of the Council of the British Interplanetary Society.

—Leslie W. Bland photo

Interview with Pioneeer "Space Doctor"

Medicine Ready to Keep Man Alive in Trip Up, Around, Down

How far has medical research moved toward safeguarding the health of the first man in orbit? What are some of the human problems of space flight? How does space medicine interrelate with the profession generally, with medical education, with allied sciences and technologies, with industries making space vehicles?

Dr. Hubertus Strughold, often called "the father of space medicine," answers these and other questions in the following wire-recorded interview with The Journal *at San Antonio, Texas, where 700 physicians and other scientists assembled several weeks ago for a symposium on the physics and medicine of atmosphere and space. Dr. Strughold was director of the Aeromedical Research Institute in Berlin before World War II. Now he is an American citizen serving as advisor for research and professor of space medicine at the School of Aviation Medicine, Randolph Air Force Base, Texas.*

Q With commercial jet aircraft now carrying humans at 35,000 ft., what kind of health dangers exist to passengers and crew?

A One danger is explosive decompression—the plane suddenly losing air pressure to the 35,000-ft. level from the comfortable cabin level of 8,000. There are measures for coping with this problem. At that altitude there are no dangers to passengers from any increased cosmic radiation. There is, however, one significant problem which arises after the flight—disruption of the normal day-night cycle.

Q Would you explain that?

A Today, it takes a propeller-driven plane about 12 hours to cross the Atlantic. In a few months, when jet airliners will begin dominating the ocean sky, it will take only six hours as the aircraft whizzes past six or seven time zones. Let us say that a passenger lands in New York at 3 p. m., when it is 9 in the evening in Europe. His appetite is thrown out of kilter. He is very sleepy and may doze off, awakening at 3 the next morning.

Q So this corresponds to sleeping and eating problems of a night worker?

A Yes, more or less, with some complexities added. Say a businessman has a very important meeting in England. Because of the upset day-night cycle he arrives unprepared, psychologically, for his work. So he should plan on arriving a few days before the meeting.

Q How does this concern the physician in practice?

A It is something he should reckon with in patients who make long overseas flights. And there is another point. Body temperature normally reaches a high around 5 in the afternoon. Suppose a man flies to New York from Paris while he has a cold, or perhaps another kind of infection. His physician finds an unusual temperature at 11 a. m. New York time when it may not be unusual at all.

Q How would space flight intensify the day-night cycle problem?

A In space travel there is no day or night. A vehicle in orbit would be 20 minutes or so in the shadow of the earth, perhaps 60 or 70 minutes in the sun's rays. So we must provide submarine conditions in creating an artificial day-night cycle.

Q What kind of submarine conditions?

A Setting periods for duty, recreation, and sleep. Submarine crews change duty every four hours, and this might be best for space crews, too. We are experimenting.

Q If technicological problems can be solved, when will we be ready—from the medical standpoint—to keep a man alive from the time of launching, through several days of orbiting, and during reentry into the atmosphere and recovery?

A We are ready now—if we can solve the recently defined problem of radiation. There are certain ways to get around that problem. One might be to launch into a route over the polar region, where it appears the radiation belt narrows. Or the vehicle velocity might be increased to shorten the time of exposure. This problem will occupy us for the next year.

Q In an interview two years ago you predicted that by the 1960's we would see 25-minute coast-to-coast flights by rocket ships looping through space. What is your estimate now?

A The same. But I was misquoted then. I said 45 minutes, not 25.

Q In the spring of 1957, before sputnik, you told THE JOURNAL [see Medicine at Work, June 15, 1957] about the space cabin simulator which nearly duplicates extraterrestrial conditions. How has that kind of study progressed?

A We now have greater knowledge of air regeneration, of carbon dioxide elimination, of the human effects of hibernation, and of the day-night cycle. So far, a man has spent seven days in the simulator. That would cover a trip to the moon. Experiments are still going on, relating to other conditions and to applications that I cannot speak about at this time. I can say, however, that we will have a space cabin simulator for two men when the special building for space medicine is completed at Brooks Air Force Base next July.

Q How might research in space medicine benefit the profession and the general public along specific medical lines—such as nutrition, psychiatry, orthopedics, physiology, pharmacology, ophthalmology, cardiology? How might physicians, generally, help solve some space medicine problems?

A A very interesting question. We will never achieve success in space flight without the vast knowledge of medicine through the ages. For example, physicians have a much better idea now about radiation than they had 5 or 10 years ago. Of course this is important in solving health problems in space flight. At the same time, the science of physiology is benefited by what we in space medicine are learning about weightlessness. And that point on cardiology—in weightlessness, we find that blood circulation is not affected very much. This is very important.

Q Do chewing, drinking, digestion, and elimination of body wastes function at zero gravity?

A With proper preparation, yes. As far as we can learn they do work—at least for short periods of time. We have reproduced weightlessness for no more than one minute for a human.

Q Are there any efforts to exchange space medicine data with Soviet physicians?

A No specific channels. They translate every paper on space medicine in the U. S.

Q How do the two countries compare in space medicine knowledge?

A The Soviets work in this field at the Institute of Aviation in Moscow and, it seems to me, at some other place. My general idea is that they are not ahead in this field—actually, they have been inspired by some events here in the United States—for example, when we rocketed monkeys into space.

Q Is there any reason to believe that the Soviets might more likely risk a man's life in order to launch him into space before we do?

A In my opinion, yes. But I also have the impression from reading the Russian medical literature, and from recent scientific conversations in Amsterdam, that they plan especially to get a dog into orbit and get the animal back.

Q What do you consider the optimum physical, mental, and emotional characteristics of the so-called premium space man?

A First let me say what I do not consider optimum—not a hermit, not a monk, not a schizophrenic. We also hear that a woman should be first in space, which would be nice and also very cavalier. But you would have to train a woman 10 years for that task. From a medical standpoint an experienced jet pilot should be first in space.

Q What other prime characteristics would be necessary?

A Motivation. He would have to want to go. He would also need to know something about the nature of space. And he would have to be familiar with medical problems in flight.

Q Would he need a personality to adapt to aloneness, or would he need to be conditioned to the problem of, as one speaker here described it, "developing an effective umbilical cord" for himself outside the earth's influence?

A I think both factors operate.

Q A little while ago you said that, from the medical standpoint, we are able to send a man up and keep him alive and well through return. Now we hear of algae as the key to a closed-cycle feeding system that will keep him nourished. How critical is this closed-cycle feeding problem?

A I don't feel that we must achieve such a system for an initial flight of, say, up to six weeks. Food can be brought along.

Q What about water?

A We have recently learned that 10% of a man's own water—called metabolic water—can be recovered daily. We can refine potable water from urine by a process that is relatively simple in a space cabin simulator. So it is not necessary to take too much water along.

Q In your experience, what manpower needs exist for the space-oriented physician as a part-time or full-time consultant in the aircraft industry?

A There is a demand for physicians of that training. Four or five years ago space medicine was a tiny part of the Air Force School of Aviation Medicine. Now almost every big company has a physician to study human factors in space flight. Convair has a physician for aeronautics and another for study of human factors.

Q Where would a physician interested in space medicine get his training?

A At the present time at Randolph, the Aeromedical Laboratory at Wright Field, or at Ohio State University. I do not believe that medical schools should establish courses in space medicine, although they might integrate the subject into the total curriculum—just as, 20 years ago, medical schools started to include lectures on aviation medicine. I think the whole field of medicine could be made much more interesting by including some phases of space medicine. The study of physiology, for example, could become really exciting if there were just a one-hour lecture on the effects of weightlessness on various body actions.

Q At this conference, participants included—besides physicians—astronomers, physicists, chemists, biologists, and representatives of other fields. Is it an advantage or a disadvantage when men of diverse disciplines meet to tackle a single problem such as space flight?

A A great advantage, definitely. In fact, this is the first time that we have had a medical meeting where at least half of the participants are not medical doctors. They are learning something from us, and we learn from them. Each is knowing where the other is trying to go.

Q What would you think is the next area for exploration involving physicians and other scientists at a future space symposium?

A Probably the same problem area as now. There might be some new problems, too, though—like antimatter, a point in physics. Time adaptation also should be discussed on a broader basis. But basically we in medicine are not so much concerned with distance as we are in duration of space flight. Our task is to develop more effective mechanisms to make longer and longer space exploration. We cannot determine the timetable. That is for the technologists and the rocket engineers.

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REPORT OF JOINT COMMITTEE ON THE NARCOTIC PROBLEM

A JOINT Committee of the American Bar Association and the American Medical Association has been engaged in a study of the narcotic problem for the past three years. Research has been conducted to ascertain the extent of this problem in those European countries equal to the United States in industrial development and to study the legal structure which these countries have erected to combat it. The present status of the narcotic problem in the United States was reviewed, and certain recommendations for further studies, both legal and medical, were made. The first report is a mine of information about the problem, and it contains much of great interest to doctors.

The situation in Europe differs from that in the United States in at least three ways: the number of known addicts is much smaller than in the United States, so the problem is far less acute; the penalties provided for persons convicted of violation of the narcotic laws are far less severe than those provided by our recent laws; there is more disposition on the part of the legal authorities to regard the problem as a primarily medical one and to turn a larger proportion of it over to the doctors.

Whether the severity of our laws is a factor aggravating or ameliorating the problem in the United States is debatable, but the question is likely to be settled by the passage of time, for Congress has recently made the laws still more severe. Certain members of the judiciary, as the Committee is advised, feel strongly that the penalties prescribed by the laws are unduly severe and that they do not have a proper relation with the penalties for other criminal offences. The mandatory sentences which these judges are required by law to pronounce are often at variance with their sense of justice, but any plan to turn over the problem to the medical profession raises the question how well this profession is prepared to deal with it. Certainly the tendency in recent years has been to increase the scope of medical efforts; for example, those suffering from undue anxiety, a subject of great interest to all doctors today, a generation ago were thought not worthy of the attention of the profession. One wonders how many physicians practicing today would welcome patients with problems concerned with addiction into their offices, or have any good idea of how to help them.

We need not accuse ourselves of lack of progress. The U. S. Public Health Service narcotic addiction hospitals at Lexington and Fort Worth are without doubt the best of their kind in the world and the research being conducted there is world-famous. We know how to withdraw addicts from their drug with safety, and we are making progress in lessening the discomforts of withdrawal, but we need to study methods of prevention. This and many other problems, such as that of relapse, cannot be successfully attacked from institutions such as Lexington and Fort Worth, where patients are seen only after they have become addicted.

To the Joint Committee it seemed obvious that the next step was to establish an experimental outpatient clinic in an urban center where addiction is prevalent, such as Washington, D. C. Such a clinic could be primarily charged with the supervision and help of former addicts discharged after withdrawal, and with patients referred to it by the courts, but this might prove to be but a small part of its activities. When it is noised abroad that there is a place to which those confronted with problems related to addiction can go for understanding and help, many may resort to it voluntarily and, if it is successful in developing practical methods, doctors would have the advantage of this experience in the handling of their own patients.

The development of a program for the intensive postinstitutional treatment of addicts has already been advocated by the Council on Mental Health of the A. M. A., and the Joint A. B. A.-A. M. A. Committee endorsed this view, recommending a limited experiment which could test various ways and means. Such a clinic could determine whether it is possible to rehabilitate addicts in a noninstitutional setting, so that they can live and function without drugs. The disciplines of medicine, psychiatry, psychology, social case work, and education should all be used. The clinic should offer psychotherapeutic guidance in dealing with their personality problems and social work help with family difficulties and vocational guidance. In short, every effort should be directed toward enabling the addict to become productive without drugs.

This may not always be as difficult as some have believed. The medical profession is most conscious of the worst side of the picture. It is the repeaters at Lexington who attract attention and provide

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The members of the Joint A. B. A.-A. M. A. Committee on Problems of Narcotic Addiction are Rufus King, Esq., Chairman; Judge Edward J. Dimock; Abe Fortas, Esq.; Dr. Robert H. Felix; Dr. Isaac Starr; and C. Joseph Stetler, Esq.

data for the literature; those who remain off the drug are hard to follow and do not appear in doctors' offices. The resolution of the House of Delegates of the A. M. A. that ambulatory treatment of addiction was impossible was passed about 35 years ago, largely as a result of acute dissatisfaction with a group of doctors making money by supplying addicts with drugs. Studies made on the adolescent addicts in New York indicate that many of them simply decide to give up the habit and do so without medical assistance of any kind. Persons lightly addicted have few withdrawal symptoms. Successful police work is reflected by the great dilution of the drugs now sold in the black market; it is more difficult to become heavily addicted than was formerly the case. Improved methods of minimizing the withdrawal symptoms, as by substituting one of the newer synthetic drugs before withdrawing, are being developed. Perhaps more patients could be successfully treated as outpatients than most now think. Certainly the psychological trauma inherent in confinement in Lexington or some similar institution should be avoided if possible.

The question of what should be done with addicts who persist in their addiction despite the clinic's best efforts leads to a controversial field where strong opinions are many and facts are few. The history of the belief that clinics for the low-cost distribution of drugs to addicts are the solution of the narcotic problem is treated at length in the joint A. B. A.-A. M. A. report. The report is clearly skeptical that any easy solution lies along those lines and agrees with the recommendation of the Council on Mental Health that the A. M. A. should not approve clinics which would dispense drugs to addicts at this time, but, like the Council on Mental Health, they were tempted by the possibility of a limited experiment conducted by experts to shed more light on this important aspect of the problem. It was the opinion of the legal members of the Joint Committee that such a test, if conducted by the experimental clinic, would not violate present laws.

The time, therefore, seems ripe for an extension of the medical attack on the narcotic problem by the establishment of outpatient clinics devoted to the problem in the centers of populations where addiction is prevalent. Indeed an outpatient clinic for addicts has already been started in New York and plans are under discussion in Philadelphia. Outpatient clinics concerned with medical counseling, chiefly for adolescents, are operating in Chicago, Detroit, and Los Angeles. The U. S. P. H. S. is embarking on a large program. One can say with confidence that such efforts seem well worthwhile.

What matter if, because of the peculiar difficulties involved, those in charge of such clinics will need the best virtues of both the doctor and the saint. The medical profession has risen to challenges before.

The Interim Report of the Joint Committee of the American Bar Association and the American Medical Association and Appendix A, "Some Basic Problems in Drug Addiction and Suggestions for Research," may be secured from Grosby Press, 30 Ferry St., New York City, at a price of $4.50.

Judge Morris Ploscowe is Director of the Narcotic Drugs Control Study instituted by the Joint Committee.

This study has been supported by a grant from the Russell Sage Foundation.

NEW AND NONOFFICIAL DRUGS, 1959

Available for the first time in January of the year of publication, the 1959 annual edition of New and Nonofficial Drugs offers practicing physicians a convenient and up-to-date compendium of the views of the A. M. A. Council on Drugs concerning most of the modern drugs in current use. In addition to revision, where necessary, of descriptions of drugs which are retained in the book for a period of 20 years, it includes new monographs that have appeared in the Council's column of The Journal since the previous edition was published. Monographs for drugs which are no longer commercially available have been deleted. The organization of contents into chapters according to the clinical application or pharmacological action of drugs has been preserved. Thus the new edition provides in cumulative, classified, indexed, and bound form a concise reference to authoritative information on newer drugs. Physicians are urged to avail themselves of the early opportunity to obtain the latest edition of the Council's annual publication by ordering it directly from the publisher, the J. B. Lippincott Company, East Washington Square, Philadelphia 5, Pa. The modest retail price of $3.35 per copy is a small investment indeed for a book which is so carefully compiled and published as an A. M. A. service to the medical profession.

In today's era of "polytherapeutics" (numerous drugs for identical or similar clinical uses) the current edition of such a book as New and Nonofficial Drugs should be almost indispensable, if not a "must," for the practicing physician. Known trade names for all described drugs are listed in conjunction with monographs, and in the index, to facilitate identification of drugs which the Council describes under recognized nonproprietary terminology. Commercially available pharmaceutical preparations, including sizes or strengths of dosage forms, also are listed in conjunction with monographs as an aid to prescribing. Most important of all—the Council's unbiased descriptions of the actions, uses, limitations, hazards, routes of administration, and dosage of drugs should enable physicians to determine their suitability for use in practice. Physicians generally also should be aware that the scope of the publication has been expanded since 1955 to encompass all individually available commercial preparations of drugs, whether or not their clinical usefulness has been established.

Physicians who have never used the Council's annual publication, or are unfamiliar with its modern features, might well consider its annual purchase as a current office guide to drug therapy.

THE PRESIDENT'S PAGE

A MONTHLY MESSAGE

For some time supporters of a movement to give hospital and medical care to social security beneficiaries have referred to the problem of the aged as primarily an economic one. Only the federal government, they contend, can cope with this large economic problem.

The American Medical Association disagrees with both allegations. Your Association's position is that the problem of senior citizens is basically a broad social one and the solutions to the many enigmas within the over-all problem must be found and implemented at the local level. Furthermore, huge federal spending cannot solve special considerations—social, psychological, physiological, and occupational—that confront our older citizens.

In this nation, perhaps in the entire world, a revolution in aging is taking place. It will affect Americans of all ages and may compare in breadth with the industrial revolution. Therefore, it is extremely important that we find out (1) the primary needs of older citizens, (2) who is responsible for meeting those needs, and (3) when they should be met —before old age or on a catch-as-catch-can basis in the critical years of senior citizenship.

Our entire thinking on the subject of aging and the aged must be as dramatic and forward-looking as the revolution itself. We dare not cling to the old perspective of aging in the face of longer life, better health, and increased productive potential on the part of our senior citizens. If we do, we will deny them and society the rewards for which medicine has fought in its war against disease.

If we separate a substantial part of our population from the rest of the human family through legislative fiat, employment and retirement policies, and community attitudes simply because they have reached a certain chronological age, we will court economic and social disaster. Simultaneously we will create an emotional problem for countless oldsters which tend to make them illness-prone.

Therefore, I believe we must begin now to give all persons—regardless of age—the full opportunity to participate in our nation's life to the extent of their desire and ability. We must eliminate present arbitrary retirement policies and other economic and social barriers to life fulfillment by the aged. We must promote health maintenance programs and wider use of restorative services, remembering that it is more desirable to restore the disabled to activity than to put them on the shelf.

We must continue to insist that adequate indigent medical care programs should be developed at the state and county level and we must reaffirm our belief that primary financial responsibility should rest with the individual, community, and state. We must have a variety of health services ready for the aged persons who need them.

We must have a nationwide educational program to demonstrate that preparation for later years must begin early—with emphasis physiologically in youth, economically during the earning period, and psychologically in middle years. We must continue to aid the voluntary health insurance industry as it develops new types of coverage for the aged.

These are just some of the positive steps that must be taken to meet the needs of older citizens in the long run, in a voluntary way and at the community and individual level. Granted it is not an easy, overnight task, and perhaps it does not have the "political appeal" of an expensive, federal medical care plan. However, I am convinced that such a program is in the best interests of all.

Gunnar Gundersen, M.D.
La Crosse, Wis.

ORGANIZATION SECTION

REGISTRATION AT THE CLINICAL MEETING, MINNEAPOLIS, DEC. 2-5, 1958

UNITED STATES

Alabama	5
Alaska	1
Arizona	2
Arkansas	6
California	49
Colorado	11
Connecticut	6
Delaware	1
District of Columbia	16
Florida	12
Georgia	3
Hawaii	1
Idaho	6
Illinois	118
Indiana	30
Iowa	108
Isthmian Canal Zone	0
Kansas	11
Kentucky	8
Louisiana	9
Maine	2
Maryland	6
Massachusetts	16
Michigan	43
Minneapolis, Minn.	662
Minnesota	772
Mississippi	5
Missouri	21
Montana	19
Nebraska	34
Nevada	5
New Hampshire	0
New Jersey	29
New Mexico	6
New York	77
North Carolina	4
North Dakota	82
Ohio	39
Oklahoma	13
Oregon	10
Pennsylvania	50
Puerto Rico	3
Rhode Island	1
South Carolina	3
South Dakota	62
Tennessee	10
Texas	35
Utah	5
Vermont	2
Virginia	6
Virgin Islands	0
Washington	23
West Virginia	9
Wisconsin	166
Wyoming	5
Total	2,628

OTHER COUNTRIES

Austria	1
Canada	21
England	1
Ireland	3
Mexico	1
Nigeria	1
Switzerland	1
Thailand	1
Total	30
	2,628
Grand Total	2,658

Numbers of Physicians and Guests Registered at Clinical Sessions

	Cleveland, Jan., 1948	St. Louis, Dec., 1948	Washington, D. C., 1949	Cleveland, 1950	Los Angeles, 1951	Denver, 1952	St. Louis, 1953	Miami, Fla., 1954	Boston, 1955	Seattle, 1956	Philadelphia, 1957	Minneapolis, 1958
Physicians												
First day	639	1,160	1,195	777	1,892	1,618	995	1,822	1,483	1,670	1,615	1,528
Second day	227	677	1,321	815	1,666	674	1,225	944	1,574	643	499	638
Two days	866	1,837	2,516	1,592	3,558	2,292	2,220	2,766	3,057	2,313	2,114	2,166
Third day	636	318	472	539	741	272	431	401	597	425	448	400
Three days	1,502	2,155	2,988	2,131	4,299	2,564	2,651	3,167	3,654	2,738	2,562	2,566
Fourth day	394	45	192	59	128	50	79	86	125	75	75	92
Four days	1,896	2,200	3,180	2,190	4,427	2,614	2,730	3,253	3,779	2,813	2,637	2,658
Guests												
First day	...*	...*	...*	736	1,499	1,667	1,199	1,852	1,732	1,164	1,537	1,206
Second day	...*	...*	...*	554	1,557	1,243	1,648	1,048	971	644	625	579
Two days	...*	...*	...*	1,290	3,056	2,910	2,847	2,900	2,703	1,808	2,162	1,785
Third day	...*	...*	...*	387	1,259	987	974	541	652	645	651	529
Three days	...*	...*	...*	1,677	4,315	3,897	3,821	3,441	3,355	2,453	2,813	2,314
Fourth day	...*	...*	...*	104	341	222	282	233	581	321	174	247
Four days	...*	...*	5,307	1,781	4,656	4,119	4,103	3,674	3,936	2,774	2,987	2,561
Technical exhibitors	...	...	...	...	...	...	674	574	730	450	936	590
Technical exhibitor's guests	...	...	...	...	...	...	209	206	192	245	340	216
Grand total	...	...	...	...	...	...	7,716	7,707	8,637	6,282	6,900	6,025

* No record.

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COUNCIL ON MEDICAL EDUCATION AND HOSPITALS

The Seventh Annual Report of the National Intern Matching Program, submitted by Ward Darley, M.D., Executive Secretary, presents information of interest to the medical profession, medical educators, hospital administrators, and prospective interns. Because this report portrays the background, development, and current status of the NIMP, the Council on Medical Education and Hospitals has requested that it be published in The Journal *of the American Medical Association.* Edward L. Turner, *M.D., Secretary.*

SEVENTH ANNUAL REPORT OF THE NATIONAL INTERN MATCHING PROGRAM

Prior to the turn of this century American medical education took very little interest in patient contact and responsibility as a part of the preparation for the practice of medicine. This lack of interest was reflected in the development of the internship as a responsibility of the hospital, rather than of the medical school, and now, more than half a century later, even though participation in and responsibility for patient care are very much a part of the medical student's education and although nearly half of the internships in the United States are in medical school affiliated hospitals, the internship continues primarily as a hospital responsibility—but a responsibility with which medical schools, and medical students as well as hospitals, are concerned. It should be of interest to review the development of this three-way concern.

Table 1.—*General Results 1952-1958*

Yr.	Hospitals Participating	Intern Programs Offered	Total Positions Offered	Total Positions Filled	% Filled	No. of Unfilled Positions	Students Participating	Students Unmatched
1952	795	1,068	10,414	5,564	53	4,850	5,681	117
1953	808	1,102	10,971	5,744	52	5,227	6,033	289
1954	820	1,032	10,729	6,051	56	4,678	6,412	361
1955	814	1,056	11,075	6,379	58	4,696	6,713	334
1956	821	1,063	11,459	6,588	57	4,871	6,821	233
1957	822	1,052	11,804	6,539	55	5,265	6,923	384
1958	819	1,062	11,958	6,734	52	5,224	7,031	397

The American Medical Association gave official recognition to the internship in 1904. The first list of hospitals approved for internship training was published in 1914. It was not until 1920 that the number of available internships began to exceed the number of medical graduates available.[1] Since 1920, and with each succeeding year, this disparity has increased until now the annual number of internships available is nearly twice the number of U. S. medical graduates. As the result of this, the development of competition between hospitals and the resultant pressures on medical students to accept internships was inevitable. As these pressures grew, it was equally inevitable that the medical schools should take an increasing interest in assisting their graduates to obtain good internships.

The first definite effort to solve this problem was in 1945 when the Association of American Medical Colleges, the American Hospital Association, the American Protestant Hospital Association, the American Catholic Hospital Association, and the American Medical Association adopted what was known as the Cooperative Plan. This plan involved the voluntary participation of medical students, medical schools, and hospitals in a complicated set of arrangements that were supposed to operate without any centralized operating authority. While the result was an improvement over the pre-1945 situation, there still remained confusion with many instances of lack of understanding and cooperation. As the number of internships continued to move ahead of the number of available U. S. graduates, it became apparent that something more was needed.

This "something" was suggested in 1950 by Dr. F. J. Mullin [2] in the form of a nationwide plan in which the matching of student and hospital choices could take place free of pressures and premature commitments, together with a time schedule and a system of appointment and acceptance notification which would be reasonable and capable of central administration. This plan was tried in 1951 and was found to be sufficiently successful so that its basic principles have been adopted as standard practice. Great credit is due the hospitals and the medical students for their willingness to cast their lot with this enterprise.

The agency now responsible for the administration of the plan is known as the National Intern Matching Program (NIMP). The NIMP is an independent corporation governed by a board of directors which has representation from the American Hospital Association, American Medical Association, American Protestant Hospital Association, Association of American Medical Colleges, Catholic Hospital Association, Student American Medical Association, and one medical student representing the medical student body at large. The Army, Navy, Air Force, Veterans Administration, and Public Health Service have liaison membership on the board.

The mechanism of the plan, although complicated in execution, is simple in theory. Basically NIMP acts as a clearing agency. Each participating student submits a confidential list to NIMP, ranking, in the order of his preference, the hospitals where he has applied for internship. He applies for any internship which interests him. Each participating hospital also submits a confidential list, ranking, in the order of its preferences, the students which have applied to it. The NIMP then matches the student with the internship he rates the highest, insofar as the hospital's relative evaluation of the student applicant makes this possible.

TABLE 2.—*Application per Student*

Yr.	No. of Students	No. of Applications	No. per Student
1952	5,681	21,728	3.8
1953	6,033	19,416	3.2
1954	6,412	21,579	3.4
1955	6,713	25,617	3.8
1956	6,821	29,471	4.3
1957	6,923	30,434	4.4
1958	7,031	32,090	4.6

TABLE 3.—*Percentage of Students Matched by Order of Choice*

Yr	First Choice	Second Choice	Third Choice	Fourth Choice or Lower
1952	84	10	3	3
1953	85	10	3	2
1954	82	11	4	3
1955	76	14	5	5
1956	74	15	6	5
1957	76	13	6	5
1958	74	14	6	6

TABLE 4.—*Hospitals Ranking of Students with Whom They Were Matched by Percentage*

Yr.	Matched from Rank Group I*	Matched from Rank Group II	Matched from Rank Group III	Other	Total
1956	61	24	11	4	100
1957	71	19	7	3	100
1958	67	22	8	3	100

*If hospital quota is 10, first 10 men on list form rank group I, numbers 11-20 rank group II, etc.

While previous reports of the NIMP[3] have given detailed descriptions of the mechanisms of matching, none are as easily understood as the one prepared by Dr. N. C. Webb Jr. at the time he was a student member of the NIMP board of directors and himself being matched to an internship.[4] The significant portion of Dr. Webb's description is reproduced herewith:

Student Confidential Preference Lists

Green	Smith	Jones
1. Mt. Sinai	1. Mt. Sinai	1. Internia
2. Internia	2. Internia	2. St. Joseph
		3. Mt. Sinai

Hospital Preference Lists

The number in parentheses shows the number of interns being sought by each hospital.

Mt. Sinai (2)	Internia (1)	St. Joseph (1)
1. Jones	1. Smith	1. Jones
2. Smith	2. Jones	
3. Green	3. Green	

Consider Green, whose first choice is Mt. Sinai, which offers two internships, and which has ranked him third. Unless either Jones or Smith get matched elsewhere, he cannot get in. He is also waiting at Internia, since it, offering but one internship, has shown preference for Smith and Jones, and, unless both Smith and Jones get matched elsewhere, Green is not in here yet either.

Consider Smith. He ranked Mt. Sinai first, and it ranked him second. Since Mt. Sinai offers two internships, Smith can be permanently "matched." Since Smith is now matched at his first choice hospital, his name is removed from Internia, his second choice, and Jones and Green slide up.

Now the situation looks like this (*indicates a permanent match):

Student Lists

Green	Smith	Jones
1. Mt. Sinai	*1. Mt. Sinai	1. Internia
2. Internia		2. St. Joseph
		3. Mt. Sinai

Hospital Lists

Mt. Sinai (2)	Internia (1)	St. Joseph (1)
1. Jones	2. Jones	1. Jones
*2. Smith	3. Green	
3. Green		

Consider Jones. Since the removal of Smith from Internia's list, Jones has moved up to top position. This is a permanent match, since it is Jones' first choice. Jones' name is removed from the Mt. Sinai list and from the St. Joseph list, since he is matched at a hospital he prefers to either of these.

Now the situation looks like this (**denotes filled hospital):

Student Lists

Green	Smith	Jones
1. Mt. Sinai	*1. Mt. Sinai	*1. Internia
2. Internia		

Hospital Lists

Mt. Sinai (2)	**Internia (1)	St. Joseph (1)
*2. Smith	*2. Jones	
3. Green	3. Green	

The removal of Jones' name from Mt. Sinai allows Green to slide up into second place. Since two internships are offered at Mt. Sinai, Green is a permanent match. Final results:

Mt. Sinai—Smith and Green
Internia—Jones
St. Joseph—none

The three students all were matched with their first choice hospital. In this example, we have seen how men "slide up" on hospital lists, as men above them are matched to hospitals more desired by those men. You will note that each man holds his positions on the lists of the various hospitals until he becomes a permanent match. No one can "by-pass" a student on a hospital list. A student is removed from a hospital list only when he is matched with a hospital he prefers more. St. Joseph got no intern because its one applicant preferred Internia and was matched there.

This, the 1958 Matching Program's report, is the seventh consecutive year in which student and hospital choices have been matched without error. The success of each matching depends on the distribution of carefully prepared materials to medical students, medical schools, and hospitals, the meeting of deadlines on the part of students, hospital administrators, medical school deans, and the NIMP office, and the careful checking and rechecking of both student and hospital choices, both with the students and hospitals and within the mechanical system of the matching itself.

Table 5.—*Major Teaching Hospitals*

Quota Saturation Percentage	1953				1958			
	No. of Hospitals	Interns			No. of Hospitals	Interns		
		Sought	Matched	% Matched		Sought	Matched	% Matched
100	39	897	897	100	45	1,224	1,224	100
99-50	58	1,962	1,457	74.3	78	2,528	1,976	78.2
49-01	40	930	289	31.1	22	526	182	34.6
0	12	87	0	0	6	47	0	0
Total	149	3,876	2,643	68.2	151	4,325	3,382	78.2

Table 6.—*Minor Teaching Hospitals*

Quota Saturation Percentage	1953				1958			
	No. of Hospitals	Interns			No. of Hospitals	Interns		
		Sought	Matched	% Matched		Sought	Matched	% Matched
100	11	177	177	100	11	145	145	100
99-50	20	271	190	70.1	25	364	265	72.8
49-01	28	403	106	26.3	13	175	38	21.7
0	20	205	0	0	8	62	0	0
Total	79	1,056	473	44.8	57	746	448	60.1

Table 7.—*Nonaffiliated Hospitals*

Quota Saturation Percentage	1953				1958			
	No. of Hospitals	Interns			No. of Hospitals	Interns		
		Sought	Matched	% Matched		Sought	Matched	% Matched
100	62	1,120	1,120	100	65	841	841	100
99-50	128	1,475	1,030	69.8	127	1,607	1,109	69.0
49-01	178	2,085	478	22.9	151	1,797	428	23.8
0	212	1,359	0	0	264	2,116	0	0
Total	580	6,039	2,628	43.5	607	6,361	2,378	37.4

The steps essential to one complete program are as follows:

1. The hospitals and students make arrangements to participate in a given program during the winter and spring before the following cycle begins. The dates indicated are approximate as they vary slightly from year to year.

2. October: The hospital directory is published, containing a description of each participating hospital, the types of internships offered and the intern quota for each.

At the same time the student directory is published which contains the name and medical school of each participating student.

3. October 1—January 10: This is the period during which the students make application for internship to hospitals. The process of application, more often than not, involves personal visits to the hospitals in which the students are interested.

4. October 1—December 10: The deans send letters of recommendation to the hospitals so that insofar as possible the hospitals may have this information when the students are interviewed or are being considered for internship.

5. January 31: Closing date for receipt at the NIMP office of student and hospital confidential rank order lists.

6. February 16: The confidential student list is confirmed to each student. Also, the confidential hospital list is confirmed to each hospital.

7. February 21: Closing date for accepting corrections to student or hospital confidential rank order lists.

8. February 23: The matching operation begins.

9. March 11: The results of the matching plan are mailed to medical school deans and to hospitals.

10. March 16: The results are given to the students by the deans. At the same time the hospitals receive their matching results.

11. March 16-26: The hospitals send contracts to matched students and students sign and return the contracts.

Except for tables 5 through 19, the tables and discussions that follow will continue the record about as it has been carried in previous reports.[5] The general statistics as shown in table 1 reveal no striking shifts over previous years. The number of unmatched students continues to be large because of the difficulty which foreign graduates have in competing with U. S. and Canadian students (152 out of all of the 397 unmatched students were graduates of foreign schools) for the more popular internships. In the program of 1959-1960 (the coming program), because screening by the Educational Council for Foreign Medical Graduates will be required for the registration of graduates from foreign schools, the number of foreign graduates participating in the program and *a priori,* the number going unmatched, will be sharply reduced. After 1959 the number of participating foreign graduates should begin to go up but also, because of the ECFMG screening, the percentage matched should be increased.

Table 2 reveals the trend for each student to apply to an increasing number of hospitals. Table 3 shows a slight continuation of the downward trend in students receiving their first choices. These two trends can be taken to indicate that students are adding, as first choice, institutions in which they may feel their chances of acceptance are open to question but also in which they would like to intern if they possibly can. A student can justify such "tries" because in doing so he knows that he is not hurting his chances for his second or third choice hospitals—hospitals which formerly he would have listed in first and second place.

Table 4 shows a slight drop in the percentage of hospitals receiving their highest choices of students. There is no logical explanation for this. The significant thing here is that the percentage of hospitals receiving the total of their first and second choices has remained essentially the same.

Tables 5 through 8 show hospitals classified according to medical school affiliation or nonaffiliation, the number of interns sought and obtained and the percentage of internships filled. The affiliated hospitals are broken down according to whether or not the degree of medical school control is of major or minor degree. The figures for the five-year period 1953 through 1958 show some very interesting trends:

Table 5, major affiliated hospitals: The total number of hospitals has remained essentially unchanged.

TABLE 8.—*Federal Services (Veteran's Administration Excluded)*

	1953				1958			
		Interns				Interns		
Quota Saturation Percentage	No. of Hospitals	Sought	Matched	% Matched	No. of Hospitals	Sought	Matched	% Matched
100	5	497	497	100	4	526	526	100
99-50	1	40	20	50	...	...	...	...
49-01	10	198	53	26.8	...	...	...	...
0	3	50	0	0	...	...	...	...
Total	19	785	570	72.6	4	526	526	100

TABLE 9.—*Hospitals Offering Stipends up to Fifty Dollars*

	1953				1958			
		Interns				Interns		
Quota Saturation Percentage	No. of Hospitals	Sought	Matched	% Matched	No. of Hospitals	Sought	Matched	% Matched
100	27	475	475	100	14	394	394	100
99-50	65	1,795	1,350	75.2	17	548	440	80.3
49-01	41	934	276	29.6	6	140	56	40
0	27	210	0	0	5	43	0	0
Total	160	3,414	2,101	61.5	42	1,125	890	79.1

TABLE 10.—*Hospitals Offering Stipends of from Fifty-one to One Hundred Dollars*

	1953				1958			
		Interns				Interns		
Quota Saturation Percentage	No. of Hospitals	Sought	Matched	% Matched	No. of Hospitals	Sought	Matched	% Matched
100	40	736	736	100	26	637	637	100
99-50	59	940	647	68.8	42	1,178	867	73.6
49-01	167	1,357	289	21.3	26	417	100	24
0	118	802	0	0	59	577	0	0
Total	324	3,835	1,672	43.6	153	2,809	1,604	57.1

The total number of interns sought and the actual percentage matched has increased. The number of hospitals filling 50% or more of their quotas has increased and those filling 49% or less has decreased.

Table 6, minor affiliated hospitals: The total number of hospitals has decreased as has also the number of interns sought. The percentage of the total of interns matched over the number sought has shown an increase. The number of hospitals filling 50% or more of their quotas has remained essentially unchanged and those filling 49% or less has decreased.

TABLE 11.—*Hospitals Offering Stipends of from $101 to $200*

Quota Saturation Percentage	1953				1958			
	No. of Hospitals	Interns			No. of Hospitals	Interns		
		Sought	Matched	% Matched		Sought	Matched	% Matched
100	36	424	421	100	53	857	857	100
99-50	74	871	614	70.5	107	1,907	1,427	74.8
49-01	83	873	237	27.1	108	1,410	350	24.8
0	88	557	0	0	173	1,310	0	0
Total	281	2,725	1,275	46.8	441	5,484	2,634	48.0

TABLE 12.—*Hospitals Offering Stipends of $201 or More*

Quota Saturation Percentage	1953				1958			
	No. of Hospitals	Interns			No. of Hospitals	Interns		
		Sought	Matched	% Matched		Sought	Matched	% Matched
100	4	62	62	100	26	302	302	100
99-50	5	39	27	69.2	62	828	593	71.6
49-01	5	56	18	32.1	43	504	136	27
0	7	28	0	0	34	254	0	0
Total	21	185	107	57.8	165	1,888	1,031	54.6

TABLE 13.—*Number of Interns Sought, from One to Nine*

Quota Saturation Percentage	1954				1958			
	No. of Hospitals	Interns			No. of Hospitals	Interns		
		Sought	Matched	% Matched		Sought	Matched	% Matched
100	42	261	261	100	29	185	185	100
99-50	58	385	258	67	56	370	246	66.5
49-01	74	487	112	23	64	445	101	22.7
0	238	1,322	0	0	193	1,159	0	0
Total	412	2,455	631	25.7	342	2,159	532	24.6

Table 7, nonaffiliated hospitals: There have been no striking changes in any of these figures over the five year span.

Table 8, federal hospitals: Veterans Administration hospitals are not included here because students apply to the individual institutions rather than to this particular governmental service. As a consequence the Veterans Administration hospitals are distributed among the previous three groupings. The only notable change in the governmental services is that the percentage of interns matched over the number sought has gone from 72.6 to 100.

Tables 9 through 12 show hospitals classified according to monthly stipends offered, the number of interns sought and obtained, and the percentage of internships filled. Here again the figures for 1953 and 1958 show significant trends.

Table 9, hospitals offering less than $50 per month: The number of hospitals, for all levels of quota saturation, has dropped precipitously. The number of interns sought and matched has also dropped throughout. On the other hand, the percentage of total interns matched over the number sought has increased.

Table 10, hospitals offering between $51 to $100 per month: Here again the total number of hospitals for all levels of quota saturation has shown a sharp drop. Except for the quota saturation of from 99 to 50%, the number of interns sought at all levels has also dropped. But the total number of interns matched has remained essentially the same and the percentage of total interns matched over the number sought has increased.

Table 11, hospitals offering between $101 to $200 per month: The number of hospitals at each saturation level has increased significantly. At all saturation levels the percentage of interns matched over the number sought has remained essentially unchanged.

Table 12, hospitals offering more than $201 per month: The number of hospitals and the number of interns sought and matched all show a very marked increase. Yet the percentage of internships filled over the number offered remains about the same.

Tables 13 through 16 show hospitals classified according to quota size, the number of interns sought and obtained, and the percentage of internships filled. It should be noted that the data cover a four-year instead of a five-year span (begins with 1954 instead of 1953).

Table 13, hospitals with from 1 to 9 interns: There has been a drop in the number of hospitals as well as in the number of interns sought at all quota saturation levels but at each level the percentage of the number of interns sought against the number matched remains essentially the same.

Table 14, hospitals with from 10 to 19 interns: The number of hospitals receiving 100% of their quotas has dropped. For each of the levels below 100%, both the number of hospitals involved and the number of interns sought has increased and yet the percentage of the number of interns sought against the number matched has remained essentially the same.

Table 15, hospitals of from 20 to 49 interns: The number of hospitals receiving 50% or more of their interns has increased and those receiving 49% or less has decreased, but at all saturation levels the percentage of the number of interns sought against the number matched has remained essentially the same.

Table 16, hospitals with 50 or more interns: The number of hospitals involved here continues to be small and none of the data for the four-year span show any significant change.

Thus, from the preceding three groups of data, it would appear (1) that the quota saturation percentage for the affiliated hospitals has been increasing and is more favorable than that for the unaffiliated; (2) that the federal services (Veterans' Administration excluded) are enjoying 100% quota saturation; (3) that, while more hospitals are offering higher stipends, the increasing high quota saturation for the low as compared to the high stipend hospitals shows that increasing numbers of graduates are attracted to an internship by factors other than stipend; and (4) that those hospitals with intern quotas of 20 or more are experiencing a much higher quota saturation than those with less.

Finally table 17 shows the distribution of the students matched as between those hospitals affiliated with their own school of graduation, hospitals not affiliated with their school of graduation but in the same state, hospitals not in the state of graduation, and the federal services (exclusive of the Vet-

TABLE 14.—*Number of Interns Sought, from Ten Through Nineteen*

	1954				1958			
		Interns				Interns		
Quota Saturation Percentage	No. of Hospitals	Sought	Matched	% Matched	No. of Hospitals	Sought	Matched	% Matched
100	69	926	926	100	56	795	795	100
99-50	86	1,111	788	70.9	107	1,453	1,031	70.9
49-01	88	1,126	259	23	102	1,358	347	25.6
0	44	529	0	0	82	975	0	0
Total	287	3,692	1,973	53.4	347	4,581	2,173	47.4

TABLE 15.—*Number of Interns Sought, from Twenty Through Forty-Nine*

	1954				1958			
		Interns				Interns		
Quota Saturation Percentage	No. of Hospitals	Sought	Matched	% Matched	No. of Hospitals	Sought	Matched	% Matched
100	29	838	838	100	33	1,009	1,009	100
99-50	43	1,287	1,004	78	55	1,648	1,292	78.4
49-01	30	880	275	31.3	17	528	142	26.9
0	2	40	0	0	3	91	0	0
Total	104	3,045	2,117	69.5	108	3,276	2,443	74.6

TABLE 16.—*Number of Interns Sought, Fifty or Over*

	1954				1958			
		Interns				Interns		
Quota Saturation Percentage	No. of Hospitals	Sought	Matched	% Matched	No. of Hospitals	Sought	Matched	% Matched
100	6	631	631	100	3	221	221	100
99-50	10	839	668	79.6	12	1,028	781	76
49-01	1	67	31	46.3	3	167	58	34.7
0	0	0	0	0	0	0	0	0
Total	17	1,537	1,330	86.5	18	1,416	1,060	74.9

erans Administration). The information really being sought here is the extent to which graduates tend to leave their own school's hospitals and communities for internship. Inspection of the table will reveal that, if the federal services are ignored, approximately half of the graduates intern outside of the state in which their school of graduation is located, one-fourth intern in the hospitals affiliated with their school of graduation, and the other fourth leave the hospitals of their school of graduation but still remain in the state.

TABLE 17.—*1958 Distribution Data—Numbers and Percentages Matched—All Schools of Medicine*

Total U. S. Graduates Matched from All Medical Schools	Hospitals Affiliated with School of Graduation		Hospitals Not Affiliated with School of Graduation but in Same State		Hospitals Out of State		Federal Service	
	No.	%	No.	%	No.	%	No.	%
6,347	1,545	24.3	1,399	22.0	2,885	45.4	518	8.16

TABLE 18.—*1958 Distribution Data—Numbers and Percentages Matched—Graduates of Privately Owned Schools of Medicine*

Total U. S. Graduates Matched from Privately Owned Medical Schools	Affiliated Hospitals of Own Medical School		Hospitals in Same State but Not Affiliated with own Medical School		Out of State Hospitals		Federal Service	
	No.	%	No.	%	No.	%	No.	%
3,451	925	26.8	651	18.9	1,641	47.6	234	6.8

Tables 18 and 19 show the breakdown of the above data as between graduates of publicly and privately owned schools. No striking difference between the two groups can be noted.

From the vantage point of seven years' perspective, it is indeed gratifying to witness the success of a complicated socioeconomic experiment of this type. It is one that justifies itself not only in the name of important service but also in the name of research data that are leading to a better understanding of a very important aspect of medical education and service.

TABLE 19.—*1958 Distribution Data—Numbers and Percentages Matched—Graduates of Publicly Owned Schools of Medicine*

Total U. S. Graduates Matched from Publicly Owned Medical Schools	Affiliated Hospitals of Own Medical School		Hospitals in Same State but Not Affiliated with Own Medical School		Out of State Hospitals		Federal Service	
	No.	%	No.	%	No.	%	No.	%
2,896	620	21.4	748	25.8	1,244	43.0	284	9.8

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COUNCIL ON INDUSTRIAL HEALTH

TONOMETRY IN GLAUCOMA SURVEYS

This report has been prepared by the Committee on Industrial Ophthalmology of the Council on Industrial Health, American Medical Association.

B. DIXON HOLLAND, M.D., *Secretary.*

The primary objective of any glaucoma survey is to discover all cases of undiagnosed glaucoma possible but not to treat, observe, or study the course of known glaucoma cases. Such a survey is most effective when the greatest number of individuals are adequately examined in the shortest possible time and with the least disturbance to their routine, by a minimum of personnel and with the minimum of equipment. The Committee feels that tonometry, the measurement of intraocular tension, is a safe procedure when properly performed by a person trained in the method and the program set up under the guidance of a consulting ophthalmologist and is the best of the various screening methods to employ in a glaucoma survey.

The members of the Committee on Industrial Ophthalmology are Edmund B. Spaeth, Chairman, Philadelphia; Franklin M. Foote, New York; Ralph S. McLaughlin, Laconia, N. H.; Joseph F. Novak, Pittsburgh; Ralph W. Ryan, Morgantown, W. Va.

BUREAU OF MEDICAL ECONOMIC RESEARCH

CRITIQUE OF SOME STATISTICS ON HEALTH INSURANCE AMONG THE AGED

Walter Polner, Ph.D., Chicago

National surveys of households now show a growing number of persons 65 years of age and over who own voluntary health insurance. By themselves, these figures on the total aged population understate the true extent of this coverage, since sizable groups among the aged do not wish to purchase this type of voluntary insurance. An analysis of these groups who have other alternatives will clarify the meaning of existing statistics on the extent of voluntary health insurance coverage of the entire aged population.

All are aware that the aged have heterogeneous attitudes toward working, housing, religion, leisure, and eating. There is little reason to believe that they maintain a homogeneous attitude toward the purchase of voluntary health insurance. Since some individuals during working life do not wish to purchase any insurance even though physically eligible and financially able, it is not surprising that there are also groups among the elderly who hold similar ideas on the purchase of voluntary health insurance. Yet there are certainly some aged who desire this insurance but are unable to obtain it; there are also some who consider that they have other means of paying for care.

The population 65 years of age and over increased to 15 million in 1958. There is every indication that this rapid change in number has brought a new interest in the study of behavior patterns of the aged. Specialists in many fields—sociologists, psychologists, political scientists, psychiatrists, economists—have presented studies on particular aspects of this increasingly important section of the population. For such specialists, however, there is a danger of considering all aged persons as identical units instead of as individuals.

The aged have two major elements in common—the number of years they have lived, which makes them alike, and the fact that they are human beings, which means they vary as widely in income, living conditions, needs, desires, and social attitudes as any other group in the population. Their earning power in the years preceding retirement varied sharply. Those who retired during the depression of the 1930's had fewer opportunities to save for old age than the wage earners now approaching retirement. The latter probably accumulated during the recent period of great postwar prosperity far more assets, such as life insurance, traditionally important in meeting the expenses of the last illness.

Consideration of the aged population as a whole, a group distinct in certain ways from the population under the age of 65, can be a valid method of studying a problem. But with a group involving so many individuals we must beware of concentrating all of our attention on this approach alone. It is only one of several ways of dealing with a question.

This warning note can well be sounded in reference to the amount of voluntary health insurance for persons 65 years of age or over. Numerous studies on the extent of voluntary health insurance for the aged have resulted in various estimates of the number of persons covered. A report from the insurance department of New York State, based on extensive studies by experts, states, "... somewhere in the order of 35 per cent of the New York State population 65 years of age and over have hospital expense insurance."[1] Such a statement from the insurance department of our most populous state carries weight, and it has been quoted extensively.[2] Even if we accept this estimate as accurate, its usefulness is doubtful unless it is taken in full context.

Voluntary health insurance is not a phenomenon related only to the age of the person covered. An understanding of voluntary health insurance coverage of the aged should include not only the numbers actually covered, but also the possible market for such coverage. How many of the aged want this insurance? How many feel no need for it, either because they can finance their own medical and hospital care or because cost of such care is met from other sources? How many are actually opposed to such insurance? Thirty-five per cent of what? These

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Research Associate, Bureau of Medical Economic Research, American Medical Association.

are questions which must be explored before any estimate of the extent of present coverage can be meaningful.

Groups Among the Aged

Who are the aged who are not interested in the purchase of voluntary health insurance? Their exact number cannot be stated, since some with alternative means of obtaining care may still purchase insurance. Some aged veterans, for instance, may be satisfied with the potential protection afforded by Veterans Administration hospitals. Other veterans may purchase insurance so that they may be assured of private treatment.

Classification of the aged into groups that are potentially outside the market for voluntary health insurance coverage can be made. Roughly five main categories seem to be involved: (1) those who receive care from local or national programs for the indigent; (2) those who receive care through some other program supported entirely by the federal government; (3) those who receive care under private nonvoluntary health insurance mechanisms; (4) those in institutions; and (5) those who oppose voluntary health insurance as a solution to their problems.

Public Aid Programs for Indigent Aged.—Persons receiving old-age assistance probably comprise the largest group outside the market for voluntary health insurance. In June, 1958, it included almost 2,500,000 individuals, few of whom have such coverage. Since there is a wide variety of medical care programs for public assistance recipients, only a few (probably less than 10%) of those indigent aged would consider it necessary to lower their standard of living by spending a portion of the assistance grant on insurance. In addition, other programs cover the aged receiving aid to the blind, aid to the totally and permanently disabled, and the indigent aged not qualified for any of the mentioned programs but aided by state and locally financed general assistance programs. For each of these groups, medical and hospital care (varying in comprehensiveness from state to state) is available at government expense.

Other Federally Supported Programs.—Groups eligible for care at federal expense are the aged veterans who consider the Veterans Administration hospital system as their "insurance" against medical expense; some dependents of servicemen who receive care through Medicare; retired military personnel as well as their dependents, especially those living near military medical facilities who can receive treatment therein; those Indians who can receive treatment under the auspices of the Division of Indian Health of the Public Health Service; merchant seamen and others eligible for care through the hospitals of the Public Health Service.

Other Programs.—There are retirees who can receive medical services as part of their retirement plans by means of insurance mechanisms other than voluntary health insurance to pay for medical and hospital service. Some firms provide employees with group life insurance which provides that the face amount may be reduced to pay hospital and medical bills. These persons have the means of payment but not "voluntary health insurance" provided for them.

Institutional Population.—The aged persons in mental and tuberculosis hospitals and sanitariums, county and state homes, government or private homes for the aged, and state or federal prisons are not now in the market for voluntary health insurance.

Opposition to Voluntary Health Insurance.—Some of the aged have religious reasons for opposition to the purchase of voluntary health insurance. They will be found among those members of religious orders which provide hospital and medical services; those with religious beliefs who do not see any necessity for voluntary health insurance; and those belonging to sects which do not consider the normal services of the physician and hospital necessary, such as various groups on the West Coast and in the Appalachian Mountain region.

Some aged are opposed to insurance per se as a means of financing any contingency, including health problems. The size of this group among the aged cannot be estimated, but it exists in the general population and, therefore, certainly carries over into the aged group.

In addition there are aged who carry insurance but not voluntary health insurance—preferring other means of meeting health costs. For such groups the idea of postpayment of medical and hospital bills may have more appeal than a prepayment system. As the working period of life recedes, the appeal of prepayment over postpayment may diminish. The use of other assets, such as savings or life insurance, may be more meaningful to them than the present voluntary health insurance system.[3]

The existence of this last group is substantiated by a recent study of the aged population of Bloomington–Normal, Ill. This study, which divided the aged population into four socioeconomic groups, indicated that proportionately less voluntary health insurance was held by the "well-to-do" group than by those in the "comfortable" income group. The author of the study states, "The few persons in Group IV [well-to-do] having insurance is probably due to the lack of concern on their part regarding medical expenses."[4] This may be an oversimplification. This "well-to-do" group may also have less inclination to use the health insurance mechanism because of their social attitude toward health insurance, their health status, their relations with physicians, and their family situation.

The question of income of the aged population is important, but dependable data on the subject are lacking. Recent studies have shown that there is a portion of the aged population having a residue of income, assets, and resources. Using income tax data as a basis for his study, Prof. James Brunner states, "These data are in apparent conflict with the general assumption that the aged either receive no *income or that the amount is very low . . . what is* also overlooked is the presence of these older persons in the higher income groups."[5] These well-to-do older people may feel less need for the insurance mechanism in meeting health needs.

Comment

These categories can probably be expanded; on the other hand, there is probably a certain amount of overlapping among the various groups listed. Exact statistics on the number of persons eligible for care through governmental or private programs or those opposed to the use of voluntary health insurance are impossible to obtain. If we consider that the largest group countable (the old-age assistance recipients) comprises almost 2,500,000 people, the maximum number of the 15 million aged persons who are now in the market for voluntary health insurance would be approximately 12,500,000. When the other aged persons in the groups listed are added to the old-age assistance group the 12,500,000 estimate will undoubtedly be very much lower. How much lower will depend on an accurate count of these aged persons. In terms of the group that believes in and is potentially in the market for health insurance coverage, elimination of these aged persons may remove a significant number from the voluntary health insurance market at the present time.

Already studies show 45% of the larger population over 60 have some type of voluntary health insurance.[6] There is a growing tendency for the group approaching retirement to hold on as much as is possible to such insurance. As more people have an opportunity to obtain this coverage in their working years and develop a belief in its usefulness, there is hope that the next decade will see most of those who desire voluntary health insurance able to obtain it at reasonable rates and without a major change in the present insurance pattern. There is also hope that those who depend on voluntary means other than health insurance also will be increasingly able to meet their medical and hospital bills during retirement without recourse to government programs. In this complex problem of the aged, "we must be wary" as Alfred North Whitehead warned, "of the error of thinking that the facts are simple because simplicity is the goal of our quest."[7] Research in this field is still difficult, and factual data are incomplete. We must continue, in his words, "to seek simplicity and distrust it."

Summary

When dealing with a large population group it is necessary to determine clearly the homogeneity of the group. The simple method of lumping together heterogeneous elements for the sake of ease of expression does not lead to understanding. It would be erroneous to believe that all the aged desire to provide for their hospital and medical bills by voluntary health insurance. Therefore, the figures on voluntary health insurance for the total aged population based on household surveys do not tell the entire story of the progress in coverage that has been accomplished in the 1950's. The resulting percentages, such as 35, are far too low, as the unmet problem is far less than 65%.

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MEDICAL NEWS

ARKANSAS

Dr. Day Goes to Washington.—The University of Arkansas Medical Center, Little Rock, held a convocation recently honoring Paul L. Day, Ph.D., member of the faculty for 31 years who has resigned to become scientific director of the U. S. Food and Drug Administration, Washington, D. C. Dr. Day has been chairman of the school's department of biochemistry since coming to Arkansas in 1927. Dr. F. Douglas Lawrason, provost for medical affairs, presided at the convocation. A faculty dinner honoring Dr. Day was held Dec. 29.

CALIFORNIA

Physicians Meeting in Palm Springs.—The American College of Physicians, Southern California Region, will meet at the El Mirador Hotel, Palm Springs, Feb. 7-8. The program has 30 papers on the scientific program, including the following:

Pre- and Post-Natal Development of the Human Lung, Dr. Clayton G. Loosli, Los Angeles.
Thyrotoxic Myopathy, Dr. Howard P. Lewis, Portland Ore.
Concepts and Misconceptions about Coccidioidomycosis and Coccidioides Immites, Dr. Roger O. Egeberg, Los Angeles.

A banquet, Feb. 7, 7:30, will have Dr. George C. Griffith, governor of the college for Southern California, as toastmaster and Horace W. Magoun, Ph.D., professor of anatomy, University of California School of Medicine, Los Angeles, speaking on "The Rise of Russian Science and Physiology." Special guests will include Drs. Dwight L. Wilbur, president, American College of Physicians, and Howard P. Lewis, president-elect of the college.

Psychiatry in General Practice.—The second Postgraduate Seminar on Psychiatry in General Practice of the Southern California Psychiatric Society, Southern California District Branch of the American Psychiatric Association, in conjunction with the General Practice Section of the Los Angeles County Medical Association will be held Jan. 31-Feb. 1 at the Los Angeles County Medical Association auditorium, 1925 Wilshire Boulevard, Los Angeles. The two-day session which will be devoted to discussions of psychiatric problems in the everyday practice of the general practitioner of medicine. Representatives of psychiatry and medicine in the Los Angeles area will speak and lead the discussions. Registration will be open to all qualified physicians and credit will be given for attendance in category II of the American Academy of General Practice. For information, write to Southern California Psychiatric Society, 427 N. Camden Drive, Beverly Hills, Calif.

Directory of Heart Clinics.—Twenty-four cardiac clinics serving heart patients in Los Angeles County have been certified by the Los Angeles County Heart Association as meeting standards to provide the best care for heart patients. The disclosure was made recently with the publication of a Cardiac Clinic Directory by the association as a community service. The heart association said 10,000 copies are being distributed without charge to physicians, nurses, and health and welfare agencies in this area. Certification of clinics, a yeararound activity of the association's Cardiac Clinics Committee, is a community service "to guarantee the best possible patient care." The directory was financed by the Wyeth Laboratories of Philadelphia. Dr. George C. Griffith, association president, said the directory reflects a nine-year effort by the association to encourage the improvement of existing facilities and the establishment of more cardiac clinics. Developed and edited by the Cardiac Clinics Committee, of which Dr. Sim P. Dimitroff is chairman, the directory serves as a guide for professional referral to clinics for children and adults. It also lists specialized services in cardiology, rheumatic fever, prophylaxis, evaluation for surgery, and cardiopulmonary function studies.

Begin Construction on Two Medical Center Buildings.—Construction of the second and third buildings of the University of Southern California Medical Center has begun. The more than 3-million-dollar project includes a six-story medical research building, a two-story instructional building, and the control center wing connecting the two. The research structure will be known as the Seeley Wintersmith Mudd Memorial Laboratory of the Medical Sciences in honor of the late Colonel Mudd, mining engineer and leading citizen of Los Angeles. It is being built with funds provided by his son, Dr. Seeley Greenleaf Mudd, vice-chairman of the board of trustees of the university and former dean of the School of Medicine, and by the U. S. Public Health Service. The basic sciences teaching building is being built with funds contributed by graduates of the School of Medicine, students, faculty members, and friends. When the buildings

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Physicians are invited to send to this department items of news of general interest, for example, those relating to society activities, new hospitals, education, and public health. Programs should be received at least three weeks before the date of meeting.

are completed in February, 1960, it will be possible for the first time for the School of Medicine to consolidate a majority of its teaching and research in one location. At present, the two years of medical instruction in the basic sciences are given on the main university park campus. The Seeley Wintersmith Mudd Memorial Laboratory Building will contain 49 laboratories, offices, and specialized chemical and physiological research facilities. The top floor has been reserved for the exclusive use of visiting scientists from this country and abroad who will be invited to lecture and to continue research work in their chosen fields at the School of Medicine. The instructional building will have 10 laboratories, two lecture rooms, anatomical laboratories, and other teaching quarters. The two buildings comprise more than 87,000 square feet of floor space, and will be completely air-conditioned.

COLORADO

Clinical Meeting in Denver.—The 24th midwinter clinical session of the Colorado State Medical Society will be held in Denver Feb. 17-20 at the Shirley Savoy Hotel. The program will feature panel discussions on "Perinatal Morbidity and Mortality" Feb. 18, with Drs. Ralph C. Benson, of Portland, Ore., and Woodruff L. Crawford, of Rockford, Ill., as guest speakers for that section. On Feb. 19, the panel will concern itself with "The Acute Abdomen," featuring Drs. Webster H. Brown, of Baltimore, and Philip Thorek, of Chicago, as guests. Feb. 20, the panel is divided into two sections, the first on wrist and ankle fractures, and orthopedic and rehabilitative problems associated with such injuries, and the second primarily concerned with the medicolegal aspects of neck injuries. Drs. William H. Bickel, of Rochester, Minn., and Miland E. Knapp, of Minneapolis, will be featured on both portions of the panel. February 17 will be devoted to an all-day orientation course for new members of the society and the opening session of the House of Delegates. Social activities are planned. Physicians in Denver during the meeting are cordially invited. A registration fee of $5 is charged all physicians.

ILLINOIS

Hospital Lecture.—The fifth lecture in the ninth annual North Shore Hospital lecture series on "Emotional Forces in the Family" will be held at the hospital, 225 Sheridan Road in Winnetka, Feb. 4, 8:00 p. m. "The Impact of Relatives and In-Laws" will be discussed by Dr. Nathan W. Ackerman, New York City, associate clinical professor of psychiatry, Columbia University, and president, Association for Psychoanalytic Medicine. The Commission on Education of the American Academy of General Practice has approved these lectures for category II credit. Dr. Ackerman has agreed to answer questions after his presentation. Physicians and allied professional personnel are invited.

KENTUCKY

Dr. Kuhns Honored.—Dr. Dwight M. Kuhns, director of laboratories, Harlan Memorial Hospital, Harlan, was presented the Carlos J. Finlay gold medal and certificate of the National Order of Merit "Carlos J. Finlay," at the Academy of Science, Havana, Cuba, Dec. 3. This award was given "for contributions to the control of meningococcal meningitis and bacillary dysentery." Carlos J. Finlay was the original author of the later proved mosquito transmission theory of yellow fever. Dr. Kuhns is a retired colonel of the U. S. Army Medical Corps.

MARYLAND

Dr. Sulzberger to Give Ketron Lecture.—The third Lloyd W. Ketron Lecture will be given by Dr. Marion B. Sulzberger Feb. 19 at Hurd Hall, Johns Hopkins Hospital, Baltimore, on "Some New Findings Concerning the Biology of the Skin Surface."

MICHIGAN

Dr. Davies Gives South American Lectures.—Dr. Windsor S. Davies, clinical professor of ophthalmology, Wayne University College of Medicine, Detroit, invited by the Pan-American Ophthalmological Society to give lectures in six South American countries, left Detroit Dec. 27 for the month-tour. He lectured before ophthalmological groups in Rio de Janeiro and Sao Paulo, Brazil; Montevideo, Uruguay; Buenos Aires, Argentina; Santiago, Chile; Lima, Peru; and Bogota, Colombia, on "Diseases of the Macula and Anterior Chamber Epithelium."

Open Center for Alcoholism.—A formal recognition program honoring the opening of a new treatment center for alcoholism was held at Wayne University College of Medicine, Detroit, Jan. 12. The Alcoholic Center, which opened Jan. 13, will be part of Receiving Hospital's outpatient clinic directed by the department of psychiatry of the university. Dr. Melvin L. Selzer, of the department of psychiatry, University of Michigan, Ann Arbor, gave a talk on "Problems of Aggression in Psychotherapy with Alcoholics." Financial backing has been given by the Michigan State Board of Alcoholism. Dr. James H. Graves, clinical director of the hospital's department of psychiatry and assistant professor at the university, will administer the program, which will give long-term and specialized care for a selected group of alcoholics. Wayne medical students participating will then evaluate different types of psychiatric treatment utilized.

MISSISSIPPI

Dr. Holland Comes to Mississippi.—Dr. William C. Holland, a member of the pharmacology department faculty at Vanderbilt University School of Medicine since 1950, has been named professor of pharmacology and chairman of the department at the University of Mississippi School of Medicine, Jackson. He replaces James C. Rice, Ph.D., who retired Dec. 31.

NEW YORK

Foreign Lecturer.—James F. Danielli, Sc.D., physiologist specializing in cytochemistry and professor of zoology, King's College, London, England, will speak at the State University Upstate Medical Center, Syracuse, March 16, 17, and 18 and will deliver a lecture the evening of March 17, 8:30 p. m., on "Designing of Drugs for the Chemotherapy of Cancer." Dr. Danielli is one of 16 scientists who will deliver Squibb Centennial Lectures in 76 medical schools this winter. E. R. Squibb and Sons has arranged the lectures to commemorate the firm's 100th anniversary.

Cardiac Teaching Day.—The third annual Cardiac Teaching Day sponsored by the Broome County Medical Society will be held Feb. 4 in the Arlington Hotel, Binghamton. Dr. Dwight E. Harken, associate clinical professor of surgery, Harvard Medical School, Boston, will present "The Pathology of Acquired Valvular Disease" and "Heart Surgery," both of which are motion-picture demonstrations. Dr. Laurence B. Ellis, associate clinical professor of medicine, Harvard Medical School, will present "Hemodynamic and Clinical Evaluation of Patients with Heart Disease" and "Late Improvement and Deterioration of Patients Who Have Had Heart Surgery." The third speaker on the program, Dr. Leroy D. Vandam, clinical professor of anesthesia, Harvard Medical School, will present "Safe Conduct of the Poor Risk Patient Through Surgery" and "Cardiac Arrest and Resuscitation." The program will conclude with audience participation and questions. For information write Mr. Charles Bishara, Executive Secretary, Broome County Medical Society, 42 Front St., Binghamton, N. Y.

New York City

Dr. Goodman Lectures in Africa.—Dr. Herman Goodman, of New York City, is visiting north and northwest Africa, the Belgian Congo, and the Indian Ocean cities of the continent January and February. He accepted invitations to informal discussions with health officials and physicians in Casablanca, Dakar, Accra, and Brazzaville. He will lecture before the local branches of the British Medical Association at Nairobi and Mombasa. Dr. and Mrs. Goodman had visited south and southeast Africa early in 1958 at the close of a round-the-world trip via Fiji, New Zealand, and Australia.

Dr. Weeden Cited.—Dr. Willis M. Weeden, medical director, Workmen's Compensation Board, New York State Department of Labor, was given a special citation "for meritorious service in appreciation of his exceptional contributions in advancing the employment of the physically handicapped." The citation, awarded by President Eisenhower's Committee on Employment of the Physically Handicapped, was presented to Dr. Weeden by Dr. Gerald D. Dorman, of New York City, chairman, New York State Medical Society's Council Committee on Workmen's Compensation, during a luncheon held as part of a two-day Institute on Workmen's Compensation.

Tuberculosis in New York City.—The number of tuberculosis deaths in New York City increased slightly in 1957, the first increase in more than a decade, according to the 1957 TB yearbook, published recently by the New York Tuberculosis and Health Association, which contains the 39th annual statistical review of this disease published by the organization. The 982 tuberculosis deaths recorded in 1957 compare with 974 in 1956. Manhattan's mortality was more marked than for the city as a whole. Whereas 365 Manhattan residents died because of tuberculosis in 1956, the number in 1957 rose to 421, an increase of 15%. During the 1957 calendar year 6,117 new tuberculosis cases were reported, compared to 6,137 the previous year. However, 16 of the city's 30 health center districts had more new cases reported in 1957 than in 1956. It was pointed out that there are certain sections of the city where the tuberculosis rate is as high, or even higher, than it was 30 years ago. Of those cases listed in the central tuberculosis register of the Department of Health on the last day of the year, 49% were residents of the Borough of Manhattan, 25% of Brooklyn, 13% of the Bronx, 12% of Queens, and 1% of Richmond.

NORTH CAROLINA

Conference on Occupational Health.—The University of North Carolina School of Medicine, Chapel Hill, will be host to the third annual Governor's Conference on Occupational Health, Feb. 5. This conference is sponsored by the North Carolina Occupational Health Council and will present a program featuring leaders in industry and industrial health in North Carolina and the nation.

Personal.—Dr. Keith S. Grimson, professor of surgery, Duke University Medical Center, Durham, has become chairman of the American Heart Association's Council for High Blood Pressure Research, succeeding Dr. Eric Ogden, of Ohio State University. Dr. Grimson served last year as vice-chairman.—Dr. Howard H. Bradshaw, director, department of surgery, Bowman Gray School of Medicine, Winston-Salem, has been named chairman of the board of governors of the American College of Surgeons. He had been secretary since 1954 and is a founding member of the North Carolina Sectional Chapter of the congress.

PENNSYLVANIA

Dr. McCall to Come to Pittsburgh.—Dr. Milton L. McCall, currently on the staff of Louisiana State University School of Medicine, New Orleans, has been appointed medical director of Elizabeth Steel Magee Hospital and chairman, department of obstetrics and gynecology, University of Pittsburgh School of Medicine. The joint appointment becomes effective July 1. Dr. McCall, who previously served on the faculty of Jefferson Medical School and on the staff of Philadelphia General Hospital, for the last five years has been head of the department of obstetrics-gynecology at Louisiana State University. He has also served as obstetrician and gynecologist in chief of the university unit of Charity Hospital in New Orleans.

Philadelphia

Campaign for I. S. Ravdin Institute.—The campaign to raise $7,300,000 for the University of Pennsylvania's I. S. Ravdin Institute and a new residence for student nurses of the Hospital of the University of Pennsylvania is being accelerated in its final seven months with more than $5,750,000 already contributed. With 78% of the goal accomplished, and anticipating raising the remainder by July 1, 1959, ceremonies were held Dec. 19 marking the beginning of demolition of the old nurses' residence to make way for the Ravdin Institute construction. Division of the funds to construct the two new buildings provides for $5,730,000 for the institute and $1,570,000 for the Hospital School of Nursing student nurses' residence. Ground was broken for the residence at the Kings Court site Nov. 25. Named for the University of Pennsylvania surgeon, Dr. I. S. Ravdin, the 224-bed institute will increase the patient capacity of the Hospital of the University of Pennsylvania to about 950. The Ravdin Institute will include laboratories for medical students and residents and special teaching facilities.

Dedicate Mental Health Center.—Pennsylvania Hospital has formally dedicated its new Mental Health Center at 49th Street and Haverford Avenue and adjoining the Institute of Pennsylvania Hospital. Ceremonies featuring Mayor Richardson Dilworth as the principal speaker climaxed plans started in 1957. The center, completed at a cost of about $3,365,000, will consolidate the hospital's West Philadelphia department formerly operated in two separate units. The new building, air-conditioned throughout, is comprised of two sections. One, a five-story wing, has accommodations for 120 patients, each room with a private bath. Dining and lounging areas are located on every floor. In another two-story section is located an "activities center," which includes a lobby, an occupational therapy department, an auditorium and gymnasium, a music room, and other facilities. Doctors' offices are also in this area. Funds were derived from several sources. Sale of the 44th Street property realized $1,173,000. A federal grant under the terms of the Hill-Burton Act supplied about one million dollars; a grant from the Ford Foundation amounted to $152,000. About $300,000 was available from other sources.

TEXAS

Symposium on DBI in Houston.—Baylor University College of Medicine with the Houston Society of Internal Medicine and the Houston Area Diabetes Association will sponsor a symposium on a new oral hypoglycemic agent, Phenformin (DBI), to be held at the Houston Academy, Feb. 5-6. The program, directed by Dr. Max Miller, Cleveland, will comprise four panel discussions on the chemistry, pharmacology, toxicology, clinicometabolic investigation and clinical evaluation of DBI in the management of diabetes mellitus, including consideration of the special problems in diabetes. More than 50 investigators in diabetes will participate in the symposium.

UTAH

Memorial Foundation.—The University of Utah College of Medicine, Salt Lake City, has announced that medical research in Utah in industrial medicine will receive impetus through the newly-organized Richards Memorial Medical Foundation, which came officially into being shortly before the death of Dr. Paul S. Richards, Sr., one of the sponsors, along with his brother, Willard B. Richards, Jr., president of the Granite Furniture Co. One of the first goals of the foundation is establishment of a professorship of occupational disease in the University of Utah College of Medicine.

WISCONSIN

Rehabilitation Center for Milwaukee.—Construction of a complete rehabilitation center within the Milwaukee County General Hospital has been announced by John W. Rankin, director of the Milwaukee County Institutions and Departments. The facility will include all physical restoration, vocational evaluation, psychological and social services, as well as an associated sheltered workshop. Applications for key positions in the rehabilitation center are being accepted as it is anticipated the center will open in the summer of this year. The center was made possible by grants from the federal and state vocational rehabilitation departments. Through the Milwaukee County institutions and departments it will be affiliated with the Marquette University School of Medicine, which plans to use it as a teaching and training center for medical students, physicians, and specialists. Dr. Robert W. Boyle, director of physical medicine, will be in charge of the facility.

GENERAL

Funds Available for Blood Research.—The Leukemia Guild of Missouri and Illinois has announced that they will have about $100,000 available for grants on July 1, to be allocated for investigative work in blood dyscrasias. Application forms are available upon request for filing on or before March 15. Applicants should include a description of research problem to be undertaken, institution in which research is to be carried out, personnel and equipment required to meet the needs of the problem, and amount of time and money needed for fruition. Requests for grants under $15,000 per year will be given preference. Address communications to: Mr. Ralph Shower, Executive Director, Leukemia Guild of Missouri and Illinois, 4530 Forest Park Blvd., St. Louis 8.

A. M. A. Grants-in-Aid for Research.—The Committee on Research of the American Medical Association has announced that the Subcommittee on Grants-in-Aid is prepared to make grants up to $500 in 1959 to supplement clinical and basic medical science research. Grants will be made for the purchase of supplies, animals, and equipment but are not intended for the payment of salaries of full- or part-time secretarial or technical help, labor or overhead. No more than two awards will be made to any one institution. The tentative closing date for the receipt of applications has been set for April 1. More complete information concerning the program and application blanks may be obtained by writing the Secretary, Committee on Research, American Medical Association, 535 N. Dearborn St., Chicago 10.

Radiology Meeting in Chicago.—The regular annual meeting of the members and fellows of the American College of Radiology will be held Feb. 6-7 at the Drake Hotel, Chicago. The afternoon of Feb. 6 a panel discussion will be conducted on the college "Principles of Ethical Radiological Practice," under the direction of Dr. Vincent W. Archer, college president. A luncheon will be given at the Drake Hotel that afternoon and the convocation that evening. The annual Teachers' Conference will be conducted Feb. 7 organized by the Committee on Education, with Dr. Philip J. Hodes as chairman. The topic will be "Radiobiology in Medicine," and 15 individual round-tables, with 10 participants per table, will be held. For information write Mr. William C. Stronach, Executive Director, The American College of Radiology, 20 N. Wacker Drive, Chicago 6.

Psychiatric Research Meeting in New York City.—The 17th scientific meeting of the Eastern Psychiatric Research Association, Inc., will be held Feb. 6, 8 p. m., at the New York University Medical School Alumni Hall A. The program will open with a film, "Migraine Equivalents." Papers will include "Empathic Communication and Anxiety in Medical Students," by Morris Weinstein, Ed. D., assistant professor of psychology, department of psychiatry, Albany Medical College, and "The Phenomenon of Chelation and Its Relation to Mental Disorders," by Dr. John C. Saunders, research scientist (pharmacology), Rockland State Hospital, Orangeburg, N. Y. Dr. Robert H. McCarter, Boston, will discuss Dr. Weinstein's paper, and Dr. George A. Jervis and Fred B. Goldstein, Ph.D., Thiells, N. Y., will discuss Dr. Saunders' paper. A business meeting will conclude the program. For information write Dr. David J. Impastato, 40 Fifth Ave., New York City, Secretary.

University Surgeons Meeting in Denver.—The 20th annual meeting of the Society of University Surgeons will be held Feb. 12-14 at the University of Colorado Medical Center, Denver, under the presidency of Dr. C. Rollins Hanlon. The program will open with addresses by Mr. Quigg Newton, president, University of Colorado; Dr. Robert Glaser, dean, University of Colorado School of Medicine; and Mr. Robert Denholm, administrator, University of Colorado Medical Center. A symposium on the "Problem of the Disappearing Service Patient in a University Surgical Training Program" the afternoon of Feb. 12 will be conducted under the chairmanship of Dr. Henry Swan, of Denver. Papers to be introduced by members include "Pituitary-Adrenal Response Following Trauma to the Isolated Leg," by Dr. R. H. Egdahl, Richmond, Va., and "Tumor-Host Relationship Factors in Man," by Drs. J. T. Grace, Jr. and A. Lehoczky, Buffalo, N. Y. The annual business meeting will be held the afternoon of Feb. 13 with the annual dinner held that evening. For information write Dr. Marshall J. Orloff, University of Colorado Medical Center, 4200 E. Ninth Ave., Denver 20, Colo.

Bahamas Medical Conference.—The seventh Bahamas Medical Conference will be held March 30-April 12 at the British Colonial Hotel, Nassau, Bahamas. The program will include the following topics and speakers:

(1) Pitfalls in the Evaluation of New Drugs; (2) New Developments in Cancer Chemotherapy, Dr. Thomas C. Fleming, Evansville, Ind.
Host Reaction in Infectious Diseases, Dr. William F. Kremer, Hartsdale, N. Y.
Epidemiology of Essential Hypertension, Dr. Marvin Moser, Valhalla, N. Y.
(1) Degenerative Vascular Changes in Diabetes; (2) Some Problems Associated with Adreno-Cortical Activity, Dr. Harold Rifkin, New York City.
(1) Congenital Aortic Stenosis; (2) Roentgenographic Aspects of Ventricular Septal Defects, Dr. Dennison Young, New York City.

Other participants include Prof. J. H. Gaddum, Cambridge, England; Dr. William L. Howell, Washington, D. C.; Brig. Gen. Thomas W. Mattingly, Washington, D. C.; Dr. Leon Unger, Chicago. Reservations should be made by writing directly to "Bahamas Conferences," P. O. Box 4037, Fort Lauderdale, Fla.

Allergy Meeting in Chicago.—The 15th annual meeting of the American Academy of Allergy will be held at the Morrison Hotel, Chicago, Feb. 9-11 with postgraduate courses presented Feb. 7 and 8. Seventeen round-table discussions will be conducted Feb. 8, 6:30 p. m. Of the 58 papers scheduled to be presented on the scientific program the following are by Canadian authors:

Cutaneous Reactions to Autologous and Non-Autologous Plasma, Drs. Samuel O. Freedman, J. Q. Bliss, J. L. Hutchison, and A. S. V. Burgen, Montreal, Quebec.
The Antigenicity of Estrone-Protein Conjugates, Dr. Bram Rose, L. Goodfriend, and A. H. Sehon, Ph.D., Montreal, Quebec.
Metabolic Studies on Asthmatic Patients Treated with Newer Steroids, Drs. Eleanor McGarry, Eleanor Venning, and Bram Rose, Montreal, Quebec.
The Effect of Ataractic and Antihistaminic Drugs on the Experimental Skin Wheal, Dr. John H. Toogood, London, Ontario.

Dr. Merle W. Moore, Portland, Ore., President, American College of Allergists, will present "More Stress on Education in Allergy," Feb. 10. Panel discussions, exhibits, and a program of social events are planned. For information write—the American Academy of Allergy, 756 N. Milwaukee St., Milwaukee 2, Wis.

Meeting on Occupational Medicine in Boston.—The 11th annual meeting of the American Academy of Occupational Medicine will be presented at the Sheraton-Plaza Hotel, Boston, Feb. 11-13, under the presidency of Dr. Ronald F. Buchan, who, with Dr. Charles C. Lund, president, Massachusetts Medical Society, will open the meeting. A discussion on "Transplantation of Normal Human Tissue—Present Status and Future" will be moderated by Dr. John P. Merrill, Boston. A field trip to the Massachusetts Institute of Technology will be conducted the afternoon of Feb. 11 under the direction of Dr. Harriet L. Hardy, of Boston. Participants include the following: Drs. Richard J. Sexton, Charleston, W. Va.; Elwood Henneman, Mark D. Altschule, Joseph E. Murray, Gustave J. Dammin, John R. Brooks, Somers H. Sturgis, Louis Weinstein, Heinrich G. Brugsch, David G. Cogan, Mary O. Amdur, Ph.D., Willem S. Frederik, Theos J. Thompson, Ph.D., Constantine Maletskos, Ph.D., and Martin Lubin, all of Boston. The annual business meeting will be held the afternoon of Feb. 12, with the annual banquet, including presentation of the academy award and the George Gehrmann Lecture, to follow at 7 p. m. A symposium on the Nuclear Reactor and Its Products will conclude the meeting.

Congress on Industrial Health in Cincinnati.—The 19th annual Congress on Industrial Health will convene in Cincinnati Feb. 16-18 at the Netherland Hilton Hotel. Three major areas of occupational health—education, research, and practice of occupational medicine—will be discussed. Sponsored by the American Medical Association Council on Industrial Health, the congress is held as a way of "furthering the development and maintenance of high medical standards in industry." The opening session Feb. 16 will be devoted to education and training in occupational health. Dr. John D. Porterfield, Washington, D. C., deputy surgeon general, U. S. Public Health Service, will speak at the annual banquet Monday evening. The Tuesday morning discussion on research in occupational health will be conducted by Dr. James H. Sterner, Rochester, New York. Poisoning resulting from industrial chemicals will be discussed Tuesday afternoon by Herbert E. Stokinger, Ph.D., Dr. A. A. Brust, and Dr. Mitchell Zavon, all of Cincinnati. A joint meeting with the Cincinnati Academy of Medicine will be held Tuesday evening when Dr. C. W. Shilling, Washington, D. C., will discuss the problem of fallout and radiation. The congress will conclude Wednesday morning with a clinical session on the practice of occupational medicine.

World Mental Health Year.—Plans for a World Mental Health Year in 1960, sponsored by 108 mental health and professional societies in 43 countries and territories, have been announced at the New York office of the World Federation for Mental Health. Following the pattern of the International Geophysical Year, the purpose of the program is "to stimulate mental health activities, including research, with a maximum of international cooperation." The federation is a nongovernmental organization which includes 29 societies in the U. S. and 79 in 42 other countries. Five major mental health objectives have been singled out for the World Mental Health Year:

1. To increase the study of child development in different countries.
2. To increase the knowledge of the many causes and the distribution of mental illness.

3. To improve and extend the teaching of the principles of mental health in medical and nursing schools, teacher-training colleges, schools of social work, theological seminaries, and similar centers of professional training.
4. To develop knowledge and techniques for dealing with the human relations problems which arise in industries and all types of occupation.
5. To encourage the study and creation of better methods of preventing and dealing with psychological problems arising from migration within and between countries, whether voluntary or involuntary.

The decision to designate 1960 as the First World Mental Health Year was taken by the executive board of the World Federation at its annual meeting at Copenhagen, August, 1957. Responsibility for financial support of plans and projects within the United States has been assumed by the World Federation for Mental Health: United States Committee, Inc.

Meeting of Orthopsychiatrists in San Francisco.—The 36th annual meeting of the American Orthopsychiatric Association will be held at the Sheraton Palace Hotel, San Francisco, March 30-31. This will be the first West Coast meeting of the association, which brings together the disciplines involved in the team approach to prevention and treatment of behavior problems and related training and research. A presidential session on the evening of March 30 will include addresses by Dr. Linus C. Pauling, Nobel laureate in chemistry and professor of chemistry, California Institute of Technology, and Weston LaBarre, Ph.D., associate professor of sociology and anthropology, Duke University, Durham, N. C. The presidential address will be delivered by Dr. Stanislaus A. Szurek, professor of psychiatry, University of California Medical School, and director of children's services, Langley Porter Neuropsychiatric Institute, San Francisco. About 60 scientific papers and 40 workshop sessions are planned, with emphasis on social and cultural aspects of mental health, treatment methods, and research. An all-day symposium is planned on brain and behavior, with the morning discussion centering on neuropsychiatry and neurochemistry and the afternoon on psychodynamic and social factors in brain damage. Four sessions are planned to include mental health films and their discussion. Exhibits related to the practice of orthopsychiatry will be on display. Information is available from Marion F. Langer, Ph.D., Executive Secretary, American Orthopsychiatric Association, 1790 Broadway, New York 19, or from the Chairman of the San Francisco arrangements committee, Dr. Donald A. Shaskan, Veterans Administration, 49 Fourth, San Francisco 3.

Papers Wanted for Congress on Industrial Health.—The Scientific Program Committee invites submission of papers for presentation at the 13th International Congress on Occupational Health in New York City at the Waldorf Astoria Hotel, July 25-29, 1960. The program will be devoted to the following aspects of occupational health:

1. Administrative Practices.
2. Medical Practices.
3. Surgical Practices.
4. Education and Training.
5. Social and Legal Aspects.
6. Environmental Hygiene.
7. Influence of Environmental Factors in Health.
8. Work Physiology and Psychology.
9. Specific Industries.
10. General.

The official languages of the congress will be English, French, German, and Spanish. However, papers may be read in the language desired by the author. Those desiring to present papers must submit abstracts (not more than 200 words, typed double-space) before Jan. 1, 1960, to Dr. Irving R. Tabershaw, Chairman of the Scientific Program Committee, 375 Park Ave., New York City. Original contributions rather than a review of previously published material will be given priority. Three copies in English are required for use by the committee and one copy in another official language of the congress. The names, academic degrees, titles, and complete addresses of author and co-author must be included in each abstract. The author who is to present the paper should be the first listed in the abstract. Complete texts of the papers in any one of the official languages must be submitted not later than April 1, 1960. The time allotted for each paper will be limited to 15 minutes, including slides. Complete papers will be published in the Proceedings of the congress.

Three Physicians Named "Outstanding Young Men."—The selection of America's Ten Outstanding Young Men of 1958 has been announced by the United States Junior Chamber of Commerce. The 10 men, all below the age of 36, were presented the silver "Jayson," symbolic of their selection by U. S. Jaycee president Robert V. Cox at Fort Lauderdale, Fla., Jan. 17. Included are three physicians: (1) Dr. James T. Grace, Jr., who reportedly described and confirmed the thesis that cancer patients retain a resistance to their tumors even when the disease becomes advanced. He conducts research at Roswell Park Memorial Institute in Buffalo, N. Y. (2) Dr. Richard T. Smith, who has made discoveries in the field of natural immunity and immunological tolerance in the newborn period of life. He is chief of pediatric services at the J. Hillis Miller Health Center, University of Florida, Gainesville. (3) Dr. Hugh E. Wilson, III, who is chairman of the division of cardiac and thoracic surgery and assistant professor of surgery at the University of Texas' Southwestern Medical School, Dallas. During the past two years, Dr.

Wilson reportedly played a leading part in building a cardiac research laboratory. Others named in the "Outstanding Young Men" group are: Lt. Shephard M. Jenks, navigator of the Nautilus submarine; Henry A. Kissinger, whose book, "Nuclear Weapons and Foreign Policy," was cited by the Overseas Press Club and awarded the Woodrow Wilson Prize; Pat Boone, singer-actor, who, while making recordings, television shows, and movies, earned a degree magna cum laude from Columbia University, New York City; Donald A. Glaser, professor of physics at the University of Michigan, Ann Arbor, who is the inventor of the bubble chamber; Warren H. Phillips, managing editor of the *Wall Street Journal;* Loran Edward Schnack, county and probate judge of Adams County, Ill.; and Gus Turbeville, president, Northland College, Ashland, Wis.

Standardization of Anesthesia Equipment.—The American Standards Association has announced that Anglo-American meetings were held in December to further the development of common standards for anesthesia and resuscitating equipment so as to make components of this equipment interchangeable in the two countries. Other nations reportedly have indicated that if the British and Americans can reach agreement, they would adopt the same standards. The six-man British delegation, representing the British Standards Institution, was headed by Dr. R. W. Cope, consultant anesthetist, University College Hospital, London, England. Leading the 30-man American delegation was Dr. Hamilton S. Davis, department of anesthesiology, Western Reserve University School of Medicine, Cleveland. Dr. Davis is chairman of the American Standards Association Sectional Committee Z79, which during the past three years has been working on standards for anesthesia equipment in this country under the sponsorship of the American Society of Anesthesiologists. Manufacturers of anesthesia equipment were represented on both delegations. Representatives of the U. S. Army, Navy, and Air Force, American Hospital Association, American Association of Nurse Anesthetists, and the Veterans Administration also participated. The manufacturers agreed to design prototype fittings, adapters, and connectors suitable for international standardization and to subject these parts within the next few months to field trials in the U. S. and Great Britain. The British, who have already tentative standards on these components, agreed to postpone formal promulgation of the standards until May, 1959, to await the outcome of these tests. Agreements made in England in July, 1958, on details of the proposed American standard for endotracheal tubes and cuffs were ratified at the meeting. This standard is essentially identical with the British proposal. The World Federation of Societies of Anesthesiologists was represented by its secretary, Dr. G. S. W. Organe, of Westminster Hospital, London.

LATIN AMERICA

Psychiatric Institute in Haiti.—The Haiti Psychiatric Institute, reportedly the first hospital in which treatment of the mentally ill will be based primarily on drug therapy, will begin operation in February, Dr. Nathan S. Kline, director of research, Rockland State Hospital, Orangeburg, N. Y., has announced. Located in Port-au-Prince, Haiti, it will be under the direction of Dr. Louis Mars, psychiatrist and minister of foreign affairs for the country of Haiti. The project is being financed by three pharmaceutical companies: Schering Corporation, Bloomfield, N. J.; Hoffmann-La Roche, Inc., Nutley, N. J.; Wyeth International, Radnor, Pa., and the Haitian government. It will be carried out under the auspices of MEDICO (Medical International Cooperation), the government of Haiti, and the Department of Mental Hygiene of the State of New York. Dr. Kline will serve as consultant to the Haitian program. In addition to financial grants to the project, the companies will provide the primary drugs to be used. Funds supplied by these companies are being used for the building of the clinic in Haiti, consisting of two wards of 10 beds each, and out-patient department, and other laboratory and administrative facilities. The government of Haiti is furnishing the land and operational funds for the project. In addition to scientific records, a sound motion picture is being made by MEDICO. For information contact: Mr. John Heyman, Coordinator, Rockland State Hospital, Orangeburg, N. Y.

FOREIGN

International Congress on Plastic Surgery.—The British Association of Plastic Surgeons is holding an international congress in London July 12-17. Subjects to be discussed include: Surgery of Congenital Deformities, Trauma of the Face, Surgery of Skin Cancer, Cosmetic Surgery, Industrial Injuries to the Hand, Anesthesia in Plastic Surgery, and Research Projects. Information may be obtained from the Organizing Secretary, Mr. David Matthews, International Congress on Plastic Surgery, c/o Institute of Child Health, Hospital for Sick Children, Great Ormond St., London, W. C. 1, England.

Congress on Fertility in Amsterdam.—The third World Congress on Fertility and Sterility, sponsored by the International Fertility Association, will be held in Amsterdam, Holland, June 7-13. The general outlines of the sections on the program will be as follows:

1. Female sterility (physiology of reproduction, pathology, endocrinology, clinical problems, treatment).
2. Male sterility (physiology of reproduction, pathology, endocrinology, clinical problems, treatment).
3. Basic research or animal reproduction.
4. Psychosexual problems.

Priority has been given to papers concerning the following subjects: embryonic death, hormonal factors and vitamins in fertility and sterility, relative value of the techniques for study of the endocrine functions in human sterility, biochemistry of spermatogenesis, and psychosexual problems in sterility. The official languages are English, German, Spanish (with simultaneous translation). Registration fee is $50 for a full member. For information and registration apply to Dr. L. I. Swaab, Honorary Secretary, Third World Congress on Fertility and Sterility, Sint Agnietenstraat 4, Amsterdam-C, Holland.

CORRECTION

Radiation Damage.—In the Foreign Letter entitled "Radiation Damages in Japanese Children" in the Jan. 3, 1959, issue of The Journal, page 62, all references to miles should have been to meters.

EXAMINATIONS AND LICENSURE

MEDICAL SPECIALTY BOARDS

American Board of Anesthesiology: *Oral.* Phoenix, April 5-10. All applications already on file. Sec., Dr. Forrest E. Leffingwell, 217 Farmington Ave., Hartford 5, Conn.

American Board of Dermatology: *Written.* Several Cities, Oct. 5. *Oral.* Oklahoma City, Jan. 15-18, 1960. The final date for filing all applications is July 1, 1959. Sec., Dr. Beatrice M. Kesten, One Haven Ave., New York 32.

American Board of Internal Medicine: *1959 Schedule—Written,* Oct. 19. Final date for filing application is May 1. *Oral.* For candidates in the South and Southwest, New Orleans, Feb. 3-6. Final date for filing application was Jan. 1. *Oral.* For candidates in the Midwest. Chicago, April 15-18. Final date for filing application was Jan. 1. *Oral.* For candidates on the West Coast. Final date for filing application is March 1. *Oral.* For candidates on the East Coast, Nov. 6-7, 9-10. Final date for filing application is March 1. *Examination in the Subspecialties. Gastroenterology.* Philadelphia, April 17-18. Final date for filing application is Feb. 1. Sec.-Treas., Dr. William A. Werrell, One West Main St., Madison 3, Wis.

American Board of Neurological Surgery: Examination given twice annually, in the spring and fall. In order to be eligible a candidate must have his application filed at least six months before the examination time. Sec., Dr. Leonard T. Furlow, Washington University School of Medicine, St. Louis 10.

American Board of Obstetrics and Gynecology: *I. Oral and Clinical.* Chicago, May 8-19. Formal notice of the exact time of each candidate's examination will be sent him in advance of the examination dates. Candidates who participated in the Part I examinations will be notified of their eligibility for the Part II examinations as soon as possible. Deadline for receipt of new and reopened application for the 1960 examinations is Aug. 1, 1959. Sec., Dr. Robert L. Faulkner, 2105 Adelbert Road, Cleveland 6.

American Board of Ophthalmology: *Oral.* Philadelphia, June 2; St. Louis, Oct. 6-10. Sec., Dr. Merrill J. King, 22 White St., Rockland, Maine.

American Board of Orthopaedic Surgery: *Part I.* Washington, D. C., Denver, Colorado and Rochester, Minn., Mar. 26-27. Deadline for filing application was Nov. 30. *Part II.* Chicago, Jan. 21-23, 1959. Deadline for receipt of applications was Aug. 15. Sec., Dr. Sam W. Banks, 116 South Michigan Avenue, Chicago 3.

American Board of Otolaryngology: *Oral.* Chicago, Oct. 5-9. Final date for filing application is February. Sec., Dr. Dean M. Lierle, University Hospitals, Iowa City.

American Board of Pathology: Boston, April 16-19. Final date for filing application is Feb. 28. Sec., Dr. Edward B. Smith, 1100 W. Michigan St., Indianapolis 7.

American Board of Physical Medicine and Rehabilitation: *Written, Part I,* and *Oral, Part II.* Philadelphia, June 12-13. Final date for filing application is February 15. Sec., Dr. Earl C. Elkins, 200 First St., S. W., Rochester, Minn.

American Board of Plastic Surgery: *Oral and Written.* Boston, May 9-11. Final date for submitting case reports is Jan. 1. Corresponding Secretary, Miss Estelle E. Hillerich, 4647 Pershing Ave., St. Louis 8, Mo.

American Board of Preventive Medicine: *Written. Public Health.* Regional, Apr. 9-11. *Occupational Medicine.* Chicago, Apr. 17-19. *Aviation Medicine.* Los Angeles, Apr. 24-26. Final date for filing application for all three examinations is Jan. 15. Sec., Dr. Tom F. Whayne, 3438 Walnut St., Philadelphia 4.

American Board of Proctology: *Oral and Written.* Philadelphia, September. Final date for filing application is March. Sec., Dr. Stuart T. Ross, 520 Franklin Ave., Garden City, N. Y.

American Board of Psychiatry and Neurology: New Orleans, Mar. 16-17; Chicago, Oct. 19-20; New York, Dec. 14-15. Training credit for full time psychiatric and/or neurologic assignment in unapproved military programs or services between the dates of Jan. 1, 1950 and Jan. 1, 1954 was terminated on Jan. 1, 1959. Sec., Dr. David A. Boyd, 102-110 Second Ave. S. W., Rochester, Minn.

American Board of Radiology: *Special Examination.* Cincinnati, Mar. 16-19, 1959. Final date for filing application was Nov. 1. *Examination.* Chicago, June 2-4. If needed a special examination will be offered at this time in Nuclear Medicine to diplomates in Radiology or Therapeutic Radiology. The deadline for filing applications is April 1. Sec., Dr. H. Dabney Kerr, Kahler Hotel Bldg., Rochester, Minn.

American Board of Surgery: *Written* examinations (Part I) will be held on December 2, 1959 at various centers to be announced later. Candidates are urged to apply several months before completion of training requirements although the closing date for filing applications is August 1. Those completing training requirements after September 30 cannot be considered for the Part I examination in December of the same year. *Part II.* New Haven, Conn., Feb. 9-10; Durham, No. Car., March 9-10; San Francisco, April 13-14; Indianapolis, May 11-12; Columbus, Ohio, May 14-15. Sec., Dr. John B. Flick, 1617 Pennsylvania Blvd., Philadelphia 3.

Board of Thoracic Surgery: *Oral.* Los Angeles, April. Final date for filing application is Dec. 1. Sec., Dr. William M. Tuttle, 1151 Taylor Ave., Detroit 2.

American Board of Urology: The oral will be given in Chicago in February 1959. Sec., Dr. William Niles Wishard, Jr., 30 Westwood Road, Minneapolis 26.

GOVERNMENT SERVICES

AIR FORCE

Personal.—At the 125th meeting of the American Association for the Advancement of Science in Washington, D. C., in December, Col. Paul A. Campbell, Chief of the Division of Space Medicine at Randolph Air Force Base, served as chairman of a joint session of the American Physiological Society and the American Astronautical Society. Among the subjects discussed at this session were: "Man-Machine Systems in Space Vehicles," "Protection of Man Against Transient Exposure to High Heat Loads," "Psychological Research on the Environment of Outer Space," and "A Comparison of Artificial Environments Used in Sealed Cabins During Flight into the Stratosphere." At the same meeting Lieut. Col. John D. Fulton, head of the school's Department of Microbiology-Cellular Biology, delivered a paper on the survival of tiny earth organisms in a simulated Martian environment. It described the colonel's work, which was carried on at the School of Aviation Medicine since 1957. In a collection of Brewer jars, the scientist simulated both soil and atmospheric conditions thought to be identical to those on Mars. Certain types of soil bacteria, placed in the jars and carefully watched over an extended period of time, survived. The project is being expanded to include such higher life forms as moss, lichens, and algae.

NAVY

Dr. Karsner Honored.—At the annual meeting of the New York Academy of Sciences in December, the title of Fellow of the New York Academy of Sciences was conferred on Dr. Howard T. Karsner, Medical Research Advisor to the Navy surgeon general. Election to Fellowship in the Academy is an honor, conferred on a limited number of members, who, in the estimation of the council, have done outstanding work toward the advancement of science.

Course in Ophthalmic Pathology.—A postgraduate course in ophthalmic pathology will convene at the Armed Forces Institute of Pathology, Washington, D. C., from March 9-13, 1959. This course will consist of a basic and comprehensive survey of pathological conditions affecting the eye. The subjects will include a review of the normal histology of the eye, changes incident to growth and aging; a review of general inflammation; acute, chronic, and granulomatous lesions and their sequelae; injuries; cataract; glaucoma; vascular diseases; intraocular tumors; and epibulbar and orbital inflammatory and neoplastic lesions. Applications from medical department officers on active or inactive duty will be forwarded through channels to the Chief, Bureau of Medicine and Surgery, Department of the Navy, Washington 25, D. C., six weeks prior to the opening date of the course. Priority will be given to officers who are board certified or board qualified, or to residents in a specialty related to the course desired.

PUBLIC HEALTH SERVICE

Examinations for Commission.—Competitive examinations for appointment to the commissioned corps of the United States Public Health Service will be held throughout the nation for physicians, April 21, 22, 23, and 24. Applications for these examinations must be filed with the surgeon general no later than March 6. Application forms and further information may be obtained by writing to the Surgeon General, U. S. Public Health Service, Washington 25, D. C. The examinations are customarily held at the Public Health Service installation nearest the applicant's home, school, or place of business. The time and place of the examinations will be announced to all applicants well in advance of the examination dates. To be eligible for appointment to the regular corps of the Public Health Service, candidates must be United States citizens, graduates of approved schools, and at least 21 years of age. Applicants who expect to meet these basic entrance requirements within nine months from the date of the written examination of choice may take the examination, but they will not be appointed to the regular corps until they have fulfilled all other requirements.

Candidates who successfully pass the entrance examination will be appointed in the grade of either the assistant or senior assistant (equivalent to Navy lieutenant, j. g., and lieutenant, or Army first lieutenant and captain). Public Health Service officers receive the pay and allowances of officers of equivalent grade in the Army, Navy, and Air Force and share many of the same benefits and privileges. Medical officers receive an extra $1,200 to $3,000 a year in incentive pay. Active duty service as a Public Health Service officer, moreover, is sufficient to satisfy Selective Service obligations under the Universal Military Training and Service Act.

DEATHS

Fenton, Ralph Albert Ⓜ Portland, Ore.; born in Lafayette, Nov. 5, 1880; Northwestern University Medical School, Chicago, 1906; since 1946 professor emeritus of otolaryngology at the University of Oregon Medical School, where he joined the faculty in 1911, and where in 1927 he became professor and head of the department of otolaryngology; member of the House of Delegates from 1932 to 1935, and chairman, Section on Laryngology, Otology and Rhinology of the American Medical Association in 1935-1936, and the following year became a member of its Board of Trustees serving until 1942; member, past-president, and vice-president of the American Laryngological Association which in 1944 awarded him its De Roaldes prize and in 1928 shared with Olaf Larsell, Ph.D., its Casselberry prize; past-president, vice-president, and secretary of the Pacific Coast Oto-Ophthalmological Society; past-president of the Portland Academy of Medicine, and Oregon Academy of Ophthalmology and Otolaryngology; member and past-vice-president of the American Academy of Ophthalmology and Otolaryngology, of which he was at one time secretary; member of the American Laryngological, Rhinological and Otological Society and from 1926 to 1930 Oregon councilor; member of the American Otological Society, Association of Military Surgeons of the United States, Chi Psi, Aero Medical Association, Nu Sigma Nu, Phi Beta Kappa, Sigma Xi, and Alpha Omega Alpha; in 1931 United States delegate to the International Congress on Military Medicine and Pharmacy at The Hague; head of the Portland chapter of the Military Order of the World War I; during World War I went overseas as a major in Base Hospital 46, serving in many of the same sectors of France as the famed 91st division; served in the Army of Occupation in Germany and rose to the rank of colonel in the Army Reserves; served as a member and director of the American Board of Otolaryngology; specialist certified by the American Board of Ophthalmology; a director of the Multnomah County Library Association from 1926 to 1953; was named for a second four-year term on the state commission for the blind in 1939 and was chosen a regent of Reed College in 1936; served on the staffs of St. Vincent's, Physicians and Surgeons, and Multnomah County hospitals, Portland Sanitarium, and Doernbecher Memorial Hospital for Children; consultant in otolaryngology to the Veterans Administration Hospital; received an honorary doctor of science degree from the University of Oregon in 1943; recently Dr. Fenton became a member of the advisory committee to the Sommer Memorial Lecture Fund endowed by the late Ernst A. Sommer of Portland for the advancement of postgraduate medical education in the Pacific Northwest; member of the editorial board of *A. M. A. Archives of Otolaryngology;* died Nov. 2, aged 77.

Ernest Edward Irons, M.D., 1877—1958.

Irons, Ernest Edward Ⓜ Chicago, President of the American Medical Association, 1949-1950, died in the Presbyterian Hospital Jan. 18, aged 81. Dr. Irons was born in Council Bluffs, Iowa, Feb. 17, 1877. He obtained his bachelor of science degree at the University of Chicago in 1900 and his doctor of medicine from Rush Medical College, Chicago, in 1903. He was awarded the degree of doctor of philosophy for research from the University of Chicago in 1912. Since 1903 he practiced in Chicago. From 1902 to 1904 he was assistant in pathology and bacteriology at the University of Chicago, under Professor E. O. Jordan. Early in his career he became associated with the Presbyterian Hospital in Chicago. From 1923 to 1936 he was dean of students and dean of the faculty of his alma mater, where for many years he was clinical professor of medicine and chairman of the department. Since 1941 he held the title of (Rush) clinical professor emeritus at the University of Illinois College of Medicine. In 1939 the Kappa Chapter of the Nu Sigma Nu Fraternity at Rush Medical College and at the University of Chicago established an annual lecture in his honor. In 1940 he gave the Charles R. Bardeen Memorial Lecture at the University of Wisconsin Medical School. Dr. Irons was elected to membership on the Council on Pharmacy and Chemistry of the American Medical Association in 1923, and served for 18 years. In 1929-1930 he was chairman of its Section on the Practice of Medicine and from 1940 to 1948 he was a Trustee. Following the death of Dr. Austin A.

Ⓜ Indicates Member of the American Medical Association.

Hayden, Dr. Irons was elected to fill the unexpired term as secretary of the Board of Trustees. In 1941 he was elected secretary of the board, serving until 1948 when he was chosen President-elect. He was a representative of the American Medical Association in the World Medical Association. He was an ex-regent of the American College of Physicians, and in 1945 president, president of the American Association for the Study and Control of Rheumatic Diseases in 1934, of the Society of Medical History of Chicago in 1940, and of the Institute of Medicine of Chicago in 1946. He was a member of the American Board of Internal Medicine, the American Rheumatism Association, Association of American Physicians, Central Society for Clinical Research, American Society for Clinical Investigation, and the American Association of Pathologists and Bacteriologists. In World War I he became colonel in command of the Base Hospital at Camp Custer near Battle Creek, Mich., and during World War II he represented medicine in many different capacities including several important committees of the National Research Council. In 1947-1948 he traveled abroad for the United States government to study health conditions. He went to Japan to recommend changes in that country's health programs for the post World War II occupation administration of Gen. Douglas MacArthur. He also made a study of medical practice in Puerto Rico. Dr. Irons was appointed by Mayor Kennelley of Chicago to the board of directors of the City of Chicago Municipal Tuberculosis Sanitarium and he became president of the board. He was consulting physician at the Presbyterian Hospital. In 1946 he was awarded the "Goldheaded Cane" of the School of Medicine of the University of California, held also by Dr. James B. Herrick, Chicago, with whom he had been associated many years. In 1958 he was presented the Chicago Medal of Merit for his contributions to the city, and the first annual Tuberculosis Institute medal in 1958 for outstanding work in the field. Distinguished for his contributions in medical research, especially in focal infection, iritis and rheumatic diseases, Dr. Irons was accorded many honors by the medical profession. His recent writings on medical economics and social medicine have been extensive and authoritative.

Johnson, Herbert William, Gorham, N. H.; Harvard Medical School, Boston, 1906; served as Gorham selectman for six years and for 27 years was an officer of the District Nurses' Association; served on the Park Commission for seven years; on the staff of St. Louis Hospital in Berlin; died Oct. 31, aged 79.

Johnson, Herman Walter Ⓜ Buffalo, N. Y.; born in Andover, Vt., Aug. 2, 1883; University of Buffalo School of Medicine, 1905; served as professor of obstetrics and chairman of the department at Baylor University College of Medicine in Houston, Texas; specialist certified by the American Board of Obstetrics and Gynecology; member of the American Association of Obstetricians and Gynecologists and the Central Association of Obstetricians and Gynecologists; fellow of the American College of Surgeons; served overseas during World War I; formerly on the consulting staff, Memorial and Herman hospitals, on the honorary staff, St. Joseph's Infirmary, and obstetrician and gynecologist-in-chief at the Jefferson Davis Hospital and the Methodist Hospital in Houston; died Nov. 13, aged 75.

Landi, Oscarre Ⓜ New York City; Regia Universita di Torino, Facolta di Medicine e Chirurgia, Italy, 1927; specialist certified by the American Board of Dermatology and Syphilology; served on the staffs of the Hospital for Joint Diseases and Mount Sinai Hospital, where he died Nov. 10, aged 55.

Pope, Emma Wightman, Carmel, Calif.; Medical Department of the University of California, San Francisco, 1899; an associate member of the American Medical Association; served as secretary of the California Medical Association; died in the Peninsula Community Hospital Nov. 1, aged 87.

Shortridge, Wilbur Holmes Ⓜ Seymour, Ind.; Indiana University School of Medicine, Indianapolis, 1935; from 1953 to 1955 a lieutenant commander in the U. S. Naval Reserve and one year aboard the USS Ajax in Far East; on the staff of the Jackson County Schneck Memorial Hospital; died Oct. 28, aged 52.

Skaggs, David Goodson, Prospect, Ky.; Hospital College of Medicine, Louisville, 1902; died in the Kentucky Baptist Hospital, Louisville, Oct. 23, aged 82.

Thomas, J. Orville Ⓜ North Branch, Mich.; Detroit College of Medicine, 1897; in June, 1949, a "Dr. Thomas Day" was held to honor him for his services; died in the Samaritan Hospital, Bay City, Oct. 20, aged 81.

Tippin, Ernest Elwood Sr. Ⓜ Wichita, Kan.; Rush Medical College, Chicago, 1920; specialist certified by the American Board of Otolaryngology; member of the American Academy of Ophthalmology and Otolaryngology and the American Society of Ophthalmologic and Otolaryngologic Allergy; veteran of World War I; associated with St. Francis and Wesley hospitals; died Oct. 30, aged 68.

Trentzsch, Max William, Highland, Wis.; University of Illinois College of Medicine, Chicago, 1913; died Oct. 29, aged 77.

Williams, Leon Arlington Ⓜ Minneapolis; University of Minnesota College of Homeopathic Medicine and Surgery, Minneapolis, 1897; died in Lester Prairie Oct. 15, aged 86.

FOREIGN LETTERS

AUSTRIA

Diagnosis of Operable Cardiac Defects.—At the meeting of the Society of Physicians in Vienna on Nov. 21, Dr. F. Grosse-Brockhoff stated that such diagnostic methods as cardiac catheterization, angiocardiography, retrograde aortography, and puncture of the left atrium and left ventricle made it possible to more accurately evaluate the significance of the symptoms. Pulmonary stenosis, aortic stenosis, patent ductus arteriosus, and tricuspid stenosis can be diagnosed with a high degree of probability by such bloodless methods as inspection, palpation, auscultation, phonocardiography, roentgenography, electrocardiography, and ultrasonic echo waves. Even if further examination with more radical and technically more complicated methods is necessary to establish the diagnosis before an operation as is the case in patients with congenital cardiac defects, the clinical diagnosis should be very much in the foreground.

Liver Function Tests.—At the same meeting Drs. R. Boller and H. Partilla said that the galactose tolerance test may yield different results, depending on whether it is performed at the usual time in the morning or whether it is started at 3 a.m. These differences depend on the condition of the patient's liver. This has a diagnostic and a prognostic significance. Patients with mild forms of hepatic diseases show lower galactose excretion if the test is started at 3 a.m. rather than at the usual hour, whereas patients with severe forms of hepatic diseases show a higher galactose excretion in the nocturnal than in the diurnal test. If serial tests are made for longer periods on patients with liver disease who show higher galactose excretion during the night compared to the day, it can be seen that even before the patients show clinical signs of improvement there is a change in the test reaction, in that the excretion of galactose during the night test decreases, whereas it increases during the day. In patients in whom the disease progresses, no such change in reaction is observed. If patients with hepatitis are treated with prednisone, a higher galactose excretion in the night is expected in those in whom prednisone has a therapeutic effect. A prompt reaction in the galactose excretion can be observed in those patients. In other words, in patients who respond to prednisone, a lower galactose excretion is expected in the nocturnal test than in the diurnal test or both tests show a negative result. The behavior of these galactose tests started at different times of the day has its explanation in the day and night rhythm.

Escape of Cerebrospinal Fluid from the Nose.—At the meeting of the Society of Physicians in Vienna on Nov. 14, Dr. D. W. Krüger stated that posttraumatic escape of cerebrospinal fluid from the nose in the early as well as the late stage should be treated surgically. In four patients escape of cerebrospinal fluid from the nose occurred after a nasal operation, due probably to a congenital defect in the lamina cribrosa. The surgical approach is mainly intradural and the defect in the lamina cribrosa may be covered with strips of fascia after the ethmoid sinuses have been evacuated and supplied with a muscle tampon. Dr. E. Wodak said that rhinologists may see patients with cerebrospinal fluid escaping from the nose after frontobasal injuries. They agree that a reparative operation should be performed if the escape of cerebrospinal fluid does not cease within a few days. Often it becomes evident that bone injuries are more diffuse than the roentgenograms indicate and the clinical findings may be obscured by giving antibiotics. The approach in patients with recent injuries is extradural. The laceration of the dura mater is closed after bony fragments have been removed. The case of a 13-year-old boy showed how important this operation is. The boy fell from a tree and did not present any symptoms. He was afebrile but had a cerebrospinal fistula. At operation, in addition to multiple fractures, a large frontal cerebral abscess was found.

JAPAN

Poliomyelitis and Salk Vaccine.—Japan is now importing Salk vaccine from the United States. The government has started to manufacture this vaccine in a pilot plant but will not be able to meet the ever-increasing demand before 1960. The incidence of poliomyelitis has practically doubled since last year. Over 2,486 cases were reported in the first 11 months of 1958.

Tuberculosis.—According to a government report, about 1 person in every 300 is actively tuberculous. About 50% of all available hospital beds are occupied by tuberculous patients. The worst aspect of the situation is that more than one-half of the very sick are not receiving proper medical attention. Although the death rate has decreased mark-

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The items in these letters are contributed by regular correspondents in the various foreign countries.

edly in the last 10 years, the number of active cases has increased by about 120,000 in the past 5 years. The reduction in the death rate, effected by the use of modern treatment methods, has occurred chiefly in the age group 20 to 24. As in some other countries, a large scale shift in incidence from youth to middle age has taken place. This may be accounted for in Japan by the following facts: Since 1951 all school children ranging in age from 6 to 15 years were examined annually. All those who had a negative reaction to tuberculin tests were given BCG vaccine and all those who had a positive reaction were x-rayed. In 1955 the basic plan of tuberculosis control was revamped to include all ages instead of being limited to those under 30.

PORTUGAL

Aspergillosis.—Cortez Pimental (*Gazeta médica portuguesa* 11:455-471, 1958) reported four new cases of pulmonary aspergillosis. The main phases of this type of aspergillosis are presence of an aspergillar mass within a preexisting cavity, atrophy and erosion of the epithelium at the level of the regions in close contact with the fungus mass, formation of a granulation tissue and its extension into the cavity, production of foreign body giant cells, and reabsorption of the micellar masses. At variance with former opinions, the author does not consider the Aspergillus as harmless, but on the other hand, he does not admit its invading properties. Its presence in the pulmonary cavity originates a pathological process similar to that caused by an intrabronchial body. Such process has a tendency to progress due to its constant growth, size, and frequency of association with secondary infection.

UNITED KINGDOM

Increase in Crime.—Mr. Butler, the Home Secretary, told the House of Commons that crime has increased by 50% in the last 20 years, the increase being greatest in the last 3 years. The chief offenders were youths between 16 and 21 years of age. There has recently been an increase in offenses committed by persons under 17. Mr. Butler said that a new research unit has been established in the Home Office for the investigation of crime and that an Institute of Criminology would soon be operating at Cambridge. The Institute for the Scientific Treatment of Delinquency also promoted scientific research into the causes and prevention of crime. This is timely, as corrective methods do not appear to prevent the increase in the number of young criminals. The clinical work of the Institute for the Scientific Treatment of Delinquency was taken over by the National Health Service 10 years ago. Its main activities are research, education, and the publication of the *British Journal of Delinquency.* The educational program is based on the view that crime is a form of behavioral disorder to be correlated with other social and psychological disorders and treated along similar lines.

Royal Commission on Doctors' Pay.—Further evidence to the Royal Commission on Doctors' and Dentists' Remuneration has been given by the Joint Consultants Committee. It suggested that the salaries of hospital medical staff should be increased by 29% to offset the fall in the value of money in the last six years and to maintain the economic standards of physicians in relation to other professions. It also recommended that the so-called distinction awards given to the top hospital consultants should be increased by 60%. If implemented, this would give an intern a salary of $1,550 a year, a consultant on the basic scale $7,600 to $11,200, and a consultant receiving the top merit award $17,800 to $22,400. The memorandum drew attention to the alarmingly high proportion of physicians attracted by prospects overseas, who are now emigrating. This in itself suggests that conditions in the National Health Service are not satisfactory. Young physicians emigrate because they object to working in a state monopoly and because financial prospects are better abroad. In one area the rate of emigration was 5 per 1,000 per year, and not all these physicians were young. Mr. Holmes Sellors, a member of the committee, referred to what he called the "inverted Micawberism" of the health service—"they are always waiting for something to turn down, rather than something to turn up."

Tuberculosis in Animals.—The danger of the dissemination of tuberculosis by domestic animals was emphasized by Dr. Soltys (*Brit. M. J.* 2:1133, 1958). There are over 10 million cattle in Great Britain and only 73% are tuberculin negative. Tubercle bacilli readily gain access to the milk, particularly if the udder is infected. Of 570 samples of milk examined by the Veterinary Investigation Center, Cambridge, 72 or nearly 13% contained tubercle bacilli. In spite of the great advances in the control of tuberculosis in cattle there will be a constant potential hazard so long as any infected animals exist. It has been proved that persons with open tuberculosis can infect cattle with the human type of baccillus. In all probability horses, sheep, and goats are not a source of danger to man, as the incidence of tuberculosis in these animals is low, but 10 to 15% of pigs in Britain are infected. The poor sanitary conditions in some slaughterhouses, and the handling of meat and organs of tuberculous animals, present a serious risk of infection for meat inspectors and slaughterhouse employees. The public health aspect of tuberculosis in dogs and cats should receive closer attention, because cats can be infected from cow's milk and dogs by contact with human cases. These animals are in close proximity to their owners and particularly to children. At present the control and prevention of animal tuberculosis is vested in the Ministry of Agriculture. All questions referring to animal diseases in relation to human health are dealt with by the Ministry of Health, but neither ministry employs a veterinarian as an advisor on veterinary matters affecting public health, as is done in some other countries.

Doctors' Hobbies.—The second Doctors' Hobbies Exhibition was opened on Nov. 10 at British Medical Association House in London. There were more than 700 exhibits by 500 physicians. The first prize ($210) was won by Dr. A. W. Fawcett, a thoracic surgeon, who exhibited a four-foot model of the torpedo-boat destroyer, Tigress, in which he once served, and which took 14 years to construct. The model has miniature recoil guns, a capstan, navigation lights, and davits to lower the lifeboats, all of which can be operated electrically. The second prize ($140) went to Dr. A. H. Wortman for a collection of stamps issued by Imperial Russia in 1858. Dr. S. Compton won the third prize ($70) for his tapestry work. An interesting exhibit was a telephone wire-tapping device, the work of Dr. Michael Ball of the Royal Air Force. He referred to this as an illegal invention and said he would not patent it, or divulge its construction, in case it fell into unscrupulous hands. The most popular exhibits dealt with photography and oil and watercolor paintings, followed by embroidery, woodwork, wood carving, and sculpture. A copy of a Stradivarius violin by Mr. Eric Peet, of the department of plastic surgery, Oxford, took 200 hours to make and was rated the best exhibit in the woodwork section. Dr. Hamilton showed a collection of 40,000 rail tickets from all over the world, including tickets to Hell and Paradise. A former vice-president of the Royal College of Surgeons, Mr. Lawrence Abel, exhibited some barber surgeons' bowls, including a Chinese one dated 1450. The exhibits covered a wide range, including a pair of tame chinchillas, popular songs, stage properties, poetry, an electronic organ, model trains and ships, ceramics, ships in bottles, and matchbox labels.

Environment and Blood Pressure.—The effect of environment on blood pressure was studied by Miall and Oldham in population samples from Rhondda Fach, a mining village in Wales, and from the Vale of Glamorgan, an agricultural area (*Clin. Sc.* 17:409, 1958). Samples chosen at random were assumed to be representative of the general population in the two districts, with their strikingly different environments. By standardizing blood pressures for age and sex, they found that a number of environmental factors have a marked influence on arterial pressure. Occupation, either directly or indirectly through economic circumstances, was found to affect it. Those in light occupations, with higher incomes, higher standards of living, and a lower energy expenditure were observed to have higher pressures than did heavy manual workers with higher expenditure of energy, lower incomes, and lower living standards. There was a steady gradation between the two extremes of activity and income. The differences were not due to differences in arm girth or weight. The effects of occupation were most noticeable in bachelors and men over 50. These were the two groups of people who most truly reflected occupational differences in income and energy expenditure. An inverse correlation was found with family size; the larger the family, the lower the blood pressure. This was true of the men as well as the married women. Single men had higher systolic pressures than did married men, and the fathers of small families had higher pressures than those of large families. This influence of family size became less obvious in elderly persons.

Typhoid from Oysters.—Six cases of typhoid reported in London have been traced to the eating of infected oysters from West Mersey, Essex. The port authority medical officer stated that the oyster fisherman must either submit their catches to bacteriological control before marketing or have a closing order issued. Many of the oysters caught in Great Britain are put through a cleansing station, and if the infection of the West Mersey oysters continues a station may be set up there. The possibility of infrared sterilization of the oysters is being considered.

Testing Rubber Gloves.—Although rubber gloves are frequently tested for perforations, this is seldom done after sterilization and never while in actual use. Small perforations are a potential source of postoperative infection, especially with staphylococci which may be present in the sweat of the surgeon's hand. Penikett and Gorrill have devised a method for testing the integrity of rubber gloves while on the operator's hands without impairing their sterility (*Lancet* 2:1042, 1958). The method is based on the insulating properties of rubber. An electrical circuit is provided with two terminals, one a pad of moistened cotton gauze, the other a heat-sterilized stainless steel bowl containing a mixture of sterile saline solution and 1% chlorhexidine solution. To test a glove, contact is made between the skin of the forehead and the gauze pad, and then each gloved hand is dipped vertically into the bowl. If there is a perforation a current flows between the two electrodes because fluid enters the perforation and robs the glove of its insulating properties. The current can be made to operate a buzzer or warning light. The chlorhexidine insures that any bacteria that do leak out are killed and do not infect gloves during the next test. If heavy infection is suspected the stainless steel bowl can be changed.

MISCELLANY

PUBLIC HEALTH SERVICE

Conference Urges More Poliomyelitis Vaccinations

In order to review the nation's experience with poliomyelitis during 1958 and to map out ways of promoting more vaccinations before next summer, Dr. Leroy Burney, surgeon general, U. S. Public Health Service, called a meeting in December in Washington, D. C., of 30 officials from national medical groups, voluntary health organizations, and state and local health departments.

The surgeon general urged parents of young children who have not been vaccinated, particularly those under five, to start their children on the course of three vaccinations immediately. Dr. Burney said, "It is a tragic circumstance that hundreds of children and young adults will be spending the balance of their lives in wheel chairs or on crutches because of a failure to be vaccinated. The parents of these children and all adults up through the age of 40 should also be vaccinated."

The primary conclusion of the conference was that intensive campaigns by local communities will be necessary throughout the coming months if millions of unvaccinated Americans under 40 years of age are to be protected before next summer. The conference stressed that such campaigns need to be organized on a block-by-block home-by-home basis. A special effort is needed, the conference agreed, to promote vaccination of children under five years of age, among whom more than half of the cases of paralytic poliomyelitis occurred this year, and of less advanced socioeconomic groups, among whom the percentage of vaccination is lowest.

There was general agreement that the point has been reached in most localities at which "face to face" campaigns under the leadership and active cooperation of local groups will be necessary to reach the "hard-to-get" segments of the population who have not responded to the poliomyelitis vaccination programs conducted by the National Foundation, the American Medical Association, the Public Health Service, and local organizations throughout the nation. "With 72 million Americans vaccinated with at least one shot, this has been one of the most successful health campaigns of recent years," said Dr. Edgar Martmer of Detroit, past-president of the American Pediatric Society, who represented the American Medical Association, "but now we need to finish the job."

The conferees urged health officials and medical societies at the county and community level to examine their local situations and determine the level of vaccination by age groups and other pertinent categories and attempt to pinpoint the factors that have prevented more complete vaccination of the most susceptible groups in their areas. Such surveys will help in planning and carrying out renewed efforts at further vaccinations. Specialists from the U. S. Communicable Disease Center reported that a survey was recently conducted in the city of Atlanta and offered the services of technicians to help other cities work out similar studies.

An important step forward, the conferees agreed, was a resolution passed Dec. 4 by the American Medical Association's House of Delegates, meeting in Minneapolis, which unanimously recommended that (1) each physician assume responsibility for making sure that all members of all families he sees are fully vaccinated; (2) that state medical societies work with state health departments to bring county and local medical societies together with health departments to work out vaccination programs; and (3) that county medical societies meet with local health departments to make surveys of local problems and devise ways to meet local situations.

The conference heard reports on the 1958 occurrence of poliomyelitis in the United States, including three epidemic areas: Detroit, New Jersey, and Virginia and nearby West Virginia; the latest data on efficacy of the vaccine; and the number of people already vaccinated, by age groups, geographic areas, and socioeconomic status.

PHS specialists from the Communicable Disease Center presented the following information on poliomyelitis in 1958:

1. There was more paralytic poliomyelitis in the United States in 1958 than in 1957, although considerably less than had occurred in any of the previous 15 years. Through Nov. 22 a total of 5,563 cases had been reported, of which 2,810 were paralytic. The poliomyelitis season in 1957 began in mid-June, somewhat later than usual, and persisted through October, with the peak in mid-September.

Attack rates this year were highest in one-year-old children, with more than 50% of all paralytic cases occurring in children under 5 years of age. The Communicable Disease Center said the figures showed a general pattern of outbreaks in urban areas, in incompletely vaccinated groups of children under 5 years of age, and in lower income groups, although there was still a sufficient number of cases outside these groups to justify urging vaccination of all persons under 40 years of age.

2. The vaccine continues to show a high rate of effectiveness. Only 12.7% of persons with paralytic cases in 1958 had received three shots of the vaccine. This is an effectiveness rate of about 87%.
3. Duration of immunity is also holding up well. From available data, the vaccine continues to be effective among persons who were vaccinated more than three years ago.

The meeting also heard detailed reports from health officials of the three epidemic areas, Detroit, which had 519 cases of paralytic poliomyelitis this year, the second worst epidemic in its experience; New Jersey, where three counties including Jersey City and Newark experienced an epidemic of 101 paralytic cases; and southwest Virginia and nearby West Virginia, where 146 paralytic cases occurred in a two-state area of 29 counties.

The PHS, it was agreed, will continue to offer aid in epidemics and in situations where epidemics are emerging; to study and maintain surveillance on the national problem; and to conduct a program of public information and education, including cooperative efforts with national organizations, to keep public attention focussed on the problem of poliomyelitis vaccination.

Attending the meeting were representatives of the American Medical Association, the American Academy of General Practice, the American Academy of Pediatrics, the Pharmaceutical Manufacturers Association, the National Foundation, the Advertising Council, Inc., and the National Health Council, in addition to state and local health department representatives and PHS staff members.

CORRESPONDENCE

WARNING AGAINST INTRATHECAL USE OF METHYLENE BLUE

To the Editor:—For at least 30 years methylene blue has been used by neurosurgeons as a dye to color the cerebrospinal fluid. In most instances the dye has been injected into hydrocephalic ventricles in the effort to demonstrate the presence or absence of a block somewhere within the ventricular system. Under these circumstances the dye becomes almost immediately very dilute. Emboldened by the use of the dye in this fashion, neurosurgeons have, on occasion, injected the dye directly or in diluted form into the lumbar subarachnoid space. We recently have used the dye in this fashion drawn from a 10-cc. ampul of aqueous 1% methylene blue solution as used intravenously. In our own case 1 cc. of the dye was diluted in 25 cc. of spinal fluid and was then injected. Shortly thereafter there was discomfort, and then followed a rather profound paraplegia, which fortunately cleared in the course of several weeks, but there was a residual perineal anesthesia and bladder dysfunction. Personal inquiry among neurosurgeons leads me to believe that this mishap has occurred in other hands as well. To date I have seen no publication bearing on the matter. The purpose of this letter is to offer an urgent word of warning against the intrathecal use of this substance.

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GOUT AFTER DIURIL THERAPY

To the Editor:—An article, "Chlorothiazide (Diuril) as a Hyperuricacidemic Agent," appeared in The Journal (168:2128-2129 [Dec. 20] 1958). I have seen two patients with typical acute gout after the initiation of chlorothiazide therapy. The serum uric acid level in each was high. In each patient there have been no recurrences for 12 and 18 months, respectively, despite maintenance doses of the drug.

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THE BIRTH AND DEATH OF SPECIALTIES

To the Editor:—Dr. Iago Galdston's paper "The Birth and Death of Specialties," which appeared on pages 2056-2061 in the Aug. 23, 1958, issue of The Journal, was read as the sixth Herman L. Reiss Memorial Lecture at the New York Academy of Medicine Building on Oct. 28, 1957, on invitation by the New York Institute of Clinical Oral Pathology. We believe that the readers of The Journal might like to have this additional information, since there was no reference to it in the footnote when the paper was published.

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MEDICAL LITERATURE ABSTRACTS

INTERNAL MEDICINE

Glutamic Acid Treatment of Hepatic Coma: Report on 10 Patients Treated and Review of 127 Cases Reported in Literature. T. Bennike. Bibl. læger 150:317-330 (No. 4) 1958 (In Danish) [Copenhagen].

Ten cases of hepatic coma in middle-aged or elderly patients were treated with glutamic acid. A certain improvement, usually transitory, resulted in half the cases. A possible precipitating factor was demonstrated in 4 of these patients. Of the 5 patients who did not respond to the treatment 4 were women past menopause. The 127 published cases of hepatic coma treated with glutamic acid during the last 3 years were mainly in patients with hepatic cirrhosis or subacute chronic hepatitis; only 15 had acute hepatitis. Improvement, usually transitory, occurred in less than half the number, but was seen in half the cases where the condition had probably been precipitated by exogenic factors. Glutamic acid treatment is symptomatic and directed to the neurologic manifestations of the hepatic coma. Ammonia intoxication is considered one of the factors in the pathogenesis of hepatic coma, but even in gravely comatose patients ammonia values in the blood may sometimes be normal. The increased ammonia concentration in the blood is presumably only an indication of a deep-seated disturbance in the N metabolism.

Malignant Pseudomembranous Staphylococcus Enteritis. E. Sivertssen and E. Juel. Tidsskr. norske lægefor. 78:993-994 (Oct. 15) 1958 (In Norwegian) [Oslo].

In the Central Hospital in Trondheim a case of malignant pseudomembranous staphylococcus enteritis in a boy aged 7 with diabetes mellitus was treated successfully. The enteritis originated 3 to 4 days after the start of tetracycline treatment for bronchopneumonia. The patient's long-continued unconsciousness is attributed mainly to a toxic effect on the cerebrum. The condition of shock with brain anoxia, dehydration, and electrolyte disturbances may have played a part. The diabetes was in the main under control and the renal function was good. Treatment of malignant pseudomembranous staphylococcus enteritis must first of all be directed to terminating the condition of shock and providing adequate supply of fluid. Immediate start of treatment with a specific antibiotic is of vital importance. Most pathogenic staphylococci are still sensitive to erythromycin, but increasing resistance is reported. The staphylococci in the case described became resistant to erythromycin after a week's treatment.

The Use of Exchange Transfusion in Acute Renal Failure. R. K. Smiley. Canad. M. A. J. 79:740-742 (Nov. 1) 1958 [Toronto, Canada].

Smiley points out that attempts to use exchange transfusion in the management of renal failure began in 1926, when Nyiri showed that cross transfusion between normal and uremic dogs would remove nitrogenous products from the uremic dogs. The first exchange transfusion in an adult was performed in France in 1947, and in 1949 Bessis recommended the exchange of the equivalent of a patient's total blood volume every 2 or 3 days in the management of renal failure. Since then the technique has been used in patients with renal failure by several French and American authors. The case reported in this paper was that of a 31-year-old woman who was hospitalized in her sixth month of pregnancy because fetal movements had not been felt for one month. Nine days after admission, the patient delivered a macerated stillborn fetus. There was no unusual bleeding and she was discharged 5 days later.

Nine days after discharge the patient was readmitted because of profuse vaginal bleeding. Dilatation and curettage of the uterus were performed at once, but bleeding continued. Continuous blood transfusions were begun, and a hysterectomy was performed. Acute renal failure with severe prolonged oliguria occurred after this patient had received 500 cc. of incompatible blood while anesthetized. The subsequent clinical course and the attendant biochemical changes were similar to those that have been described in many patients with acute renal failure of diverse etiology. The presence of decreased prothrombin activity and thrombocytopenia with a markedly prolonged bleeding time during the bleeding phase immediately after infusion of the incompatible blood was

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The place of publication of the periodicals appears in brackets preceding each abstract.

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confirmed. Measurements of plasma fibrinogen were not made, but the coagulation time was normal and a firm clot formed.

Exchange transfusion was performed on the 15th day of oliguria when the patient's condition, characterized by coma and repeated convulsions, was judged to be desperate. These serious manifestations disappeared during the exchange procedure and did not recur although the urine output did not exceed 500 cc. until the fifth day after the exchange transfusion. After that the patient became progressively more alert. Her convalescence was slow and marked by polyuria and thirst. Five months after the episode of renal failure, the patient was asymptomatic. Routine examinations of the blood and urine revealed normal results. While the French investigators had suggested that the exchange procedure be repeated every second day in order to remove an amount of urea calculated to be equal to the amount which would be produced in 2 days, in the case reported here, the improvement was maintained throughout the subsequent days of oliguria, and so the procedure was not repeated.

SURGERY

The Patella in Degenerative Joint Disease: A Clinicopathologic Study. R. A. Haliburton and C. R. Sullivan. A. M. A. Arch. Surg. 77:677-683 (Nov.) 1958 [Chicago].

A total of 154 patellectomies were performed on 136 patients with degenerative disease of the patellofemoral joint at the Mayo Clinic between 1950 and 1954. There were 85 female and 51 male patients between the ages of 15 and 58 years. The patients complained of pain, and associated complaints were locking, instability, stiffness, crepitus, and swelling. Physical findings were tenderness, crepitus, effusion, and limitation of motion. Forty-five patients had a history of trauma, and 20 had one of recurrent dislocation of the patella. Seventy-two patients were 30 lb. (13.6 kg.) or more overweight. One hundred nineteen patellas removed from 41 male and 68 female patients (with both patellas removed from 10) were subjected to pathological examination and graded according to the degree of degenerative change. Twenty-eight patellas were classified as grade 1, i. e., cartilage degeneration with absence of or slight marginal hyperplasia; 58 patellas showed grade 2 cartilage degeneration with well-marked marginal hyperplasia, and 33 grade 3 with gross distortion in the shape of the patella, with eburnation of the articular surface. Seventy-four of the 109 patients were followed up for 2 to 7 years after the patellectomy; in general the patients were well satisfied with the results of the surgical measures, and the patients who had patellar degeneration of grade 3 were the most satisfied group.

Advanced degenerative disease of the patellofemoral joint is commoner among women than among men. The patellas of these patients are worn out on the lateral side and have a characteristic appearance. The higher incidence among women is probably the result of increased tendency for the patella to displace laterally, either from dysplasia of the joint or from the more acute valgus alignment of the knee in women. Patellectomy for degenerative joint disease gives subjective improvement in a high proportion of patients, particularly those with advanced disease.

Extrapleural Pneumolysis and Pulmonary Tuberculosis: Preliminary Hospital Results in a Series of 200 Cases. G. G. I. Gordon. East African M. J. 35:527-532 (Sept.) 1958 [Nairobi, Kenya].

The author reports on 200 consecutive patients, between the ages of 12 and 74 years, who underwent extrapleural pneumolysis for pulmonary tuberculosis and were followed up postoperatively for periods varying from a few months to about 2½ years. In general, the operation was performed on patients with disease severely affecting the upper lobe, with or without lesions in other areas. The relative indications were failure of antibiotic therapy, failure of artificial pneumothorax or pneumoperitoneum, and persistent hemoptysis when uncontrolled by other measures. Full antibiotic cover was considered essential, both during and after the surgical intervention. Surgical complications were as follows: Marked hemorrhage into the extrapleural space, requiring blood transfusion, occurred in 7 patients; severe surgical emphysema occurred in 6 patients, contralateral spread in 6 patients, air embolism in 5 patients, tuberculous infection of the extrapleural space in 5, pyogenic infection of the space in 4, and serious mental symptoms in 2. Eleven patients died, representing an operative mortality of 5.5%. Death resulted from air embolism in 3 patients, from anesthesia in 2, from respiratory failure in 2, from tuberculous empyema in 2, from pulmonary embolism in 1, and from hemoptysis in 1. Considering the fact that most of the patients had extensive pulmonary tuberculosis which had not responded to prolonged routine therapy and that the operation was often performed on a last-hope basis, this mortality rate seems low. Conversion of the sputum from positive to negative resulted in 179 patients (89%). This greatly exceeded the sputum conversion rate among patients treated by administration of antibiotics and simple collapse methods. Ten patients were therapeutic failures.

The early results obtained in these patients are encouraging and extrapleural pneumolysis, therefore, is considered to have a definite place in the treatment of the African with pulmonary tuberculosis. Extrapleural pneumolysis is perhaps the simplest of the major surgical interventions used in the treatment of pulmonary tuberculosis. It is of particular value in undeveloped countries in which the facilities for resection are not readily available. It may be indicated in patients in whom resection cannot be performed, as in those with disseminated lesions or with greatly reduced respiratory capacity.

Sudeck's Atrophy and the Shoulder-Hand Syndrome. J. G. Taylor. Proc. Roy. Soc. Med. 51:879-883 (Oct.) 1958 [London].

The author believes that Sudeck's atrophy (patchy bone atrophy [osteoporosis] after injury) and the shoulder-hand syndrome (Steinbrocker 1947) are related conditions. He discusses 10 cases of Sudeck's atrophy and 6 of the shoulder-hand syndrome. Sudeck's atrophy occurs most commonly after injury in the vicinity of the wrist or ankle joints. In this series fracture of the lower end of the radius was the usual preceding injury. There are 4 characteristic features of the conditions: loss of motor function, pain, vasomotor disturbance, and osteoporosis. After the causative injury there is usually early swelling with difficulty in finger or toe movements; there is diffuse pain in the hand and wrist (or foot and ankle) which is not relieved by immobilization; the extremity becomes hot, red, and puffy with loss of the normal fine creases in the skin; hyperesthesia or paresthesia may be present; there is increasing stiffness of hand or foot in which spasm seems to play a part. When the complication follows a Colles' fracture the symptoms may declare themselves soon after the injury or not become manifest until after the plaster is removed. Osteoporosis is obvious at about 6 weeks. The osteoporosis affects the cancellous tissue of the carpus, the lower ends of the radius and ulna and the extremities of the metacarpals and phalanges, and later their shafts. In the foot the corresponding bones are affected.

The shoulder-hand syndrome is a more extensive disability. Sometimes the disability of the hand may precede that of the shoulder, but usually for the first few weeks or months there is a painful, stiff, tender shoulder and a hyperemic swollen, painful hand with smooth taut skin and limited finger movement. Sometimes, however, the hand may be cold, purple, and sweating. Thereafter the disorder may resolve, or diffuse pain in the shoulder and arm may persist with increasing atrophic changes, stiffness, and osteoporosis of the hand, but decrease of swelling, and coldness instead of heat. The final stage is one of permanent disability, but it may resolve spontaneously. The shoulder-hand syndrome sometimes follows injury such as a tear of the rotator cuff, but it has been observed also after myocardial infarction, hemiplegia, cervical nerve root irritation, or herpes zoster.

Of the 10 cases of Sudeck's atrophy observed by the author 9 occurred in women, 8 of them after fracture of the wrist. In 4 of the 6 patients with the shoulder-hand syndrome the disorder was preceded by injury to the shoulder, in 1 by a cardiac infarct and in 1 no etiological factor was found. The treatment is the same for both conditions. Elevation was used to reduce swelling of the hand and the patients were instructed to perform such finger, hand, and shoulder movements as they could do without increasing their pain. During the stage of spontaneous pain physiotherapy and intensive active exercises aggravated the symptoms. When the pain had subsided, wax baths and active exercises became helpful in restoring movement. Sympathetic ganglion block, carried out in the severe cases, produced permanent improvement in only 1 of the patients. In the others the effect was only temporary. Cortisone therapy was tried in 3 patients; it failed in 2 patients with the shoulder-hand syndrome, but produced improvement and finally recovery in a patient with Sudeck's atrophy. The final outcome was fairly satisfactory, in that 6 of those with Sudeck's atrophy recovered in about 10 months; in 3 slight disability remained, and in 1 severe disability. Of the 6 patients with the shoulder-hand syndrome 4 made a complete recovery, 1 has slight residual stiffness, and 1 had severe shoulder and hand disability after 2 years.

Chemopallidectomy for Relief of Parkinson's Disease with Remarks on Selection of Cases for Operation and Improvements in Surgical Technique. J. M. Meredith. J. South Carolina M. A. 54:357-363 (Oct.) 1958 [Florence].

The most hopeful approach to the neurosurgery of Parkinsonism is destructive chemical surgery of the basal ganglia, particularly of the globus pallidus or portions of the thalamus. The majority of neurosurgical clinics in this country favor either (1) chemopallidectomy by means of alcohol injection into the basal ganglia, or (2) the pallidotomy knife-cutting technique of McKinney. Ultrasound techniques that are utilized now in some of the research centers are so elaborate and time-consuming that they are not very practical and feasible for most hospitals in which Parkinsonism patients are being operated on.

With reference to the selection of patients with Parkinson's disease for chemopallidectomy, the most important contraindications are pseudobulbar symptoms, mental deterioration, vegetative signs, spontaneous hyperthermia and excessive sweating and salivation, respiratory difficulties such as uncontrollable hyperpnea, and psychiatric disorders. Physiologic signs of senility also contraindicate surgery, but chronologic aging, per se, does not. Parkinsonian patients with unilateral or bilateral symptoms and none of the foregoing contraindica-

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of 50 and 70 years. Fifty-three patients (44.1%) had obtained excellent results, 32 (26.6%) good results, 21 (17.5%) satisfactory results, and 14 (11.8%) poor results. Only 21 (17%) of the 120 patients complained of residual back pain. Adding spine stabilization procedures to simple disk excision did not cause any increased incidence of morbidity in this series of patients as compared with those undergoing only a simple disk excision. The average duration of the patient's stay in the hospital was 18.4 days, which was not much longer than that of patients on whom only the simple procedure was performed. The results obtained were far from perfect but with increased attention to the finer details of spine fusion technique they can be improved. Although some of the patients exhibited a pseudarthrosis, these spines were remarkably stable due to dense fibrous tissue formation resulting in a decrease in back pain.

Surgeons who evaluate end results on a basis of relief of sciatica alone tend to ignore a major disability factor. Backache is the cause of more chronic disability than nerve pain from sciatica. No end-result study can be accepted unless it is based on an evaluation at least 4 to 5 years after surgical intervention. The reported data suggest that a spine fusion procedure should be performed on all patients from whom a ruptured or herniated intervertebral disk is removed. Most patients with simple disk excision will undergo subsequent degenerative changes in the facet joints of the lumbar spine. Patients who have had a disk removed and later require a fusion dread the second operation much more than the first, and all degrees of anxiety and psychoneurosis may be seen in these patients. The authors have been unable to arrive at any reliable criteria for differentiating among those patients who will not need spine stabilization and those in whom back pain will be so incapacitating that a second operation for spine stabilization should be performed. Pantopaque, although believed to be rapidly absorbed in the subarachnoid space, was observed to be present in significant amounts as long as 10 years after myelography. However, no significant reactions were noted to the prolonged presence of the Pantopaque mediums.

Sarcoidosis of the Small Intestine (Its Relation to Crohn's Regional Ileitis). M. Janbon and L. Bertrand. Presse méd. 66:1491-1494 (Oct. 1) 1958 (In French) [Paris].

The authors report on a 30-year-old woman in whom a progressive obstruction of the small intestine developed while she was subjected to a combined antituberculous treatment for acute miliary tuberculosis of the lungs. Mycobacterium bacilli were absent in the sputum, in the gastric juice, and in the feces; repeated tuberculin tests were negative. Roentgenograms of the gastrointestinal tract made during the subacute phase of bowel obstruction showed delayed passage and considerable dilatation alternating with narrowing of the jejunoileal loops. Roentgenograms of the chest did not show any pulmonary lesion which was seen two months previously, thus the antituberculous treatment seemed to have completely and spontaneously cured the acute miliary tuberculosis of the lungs. Laparotomy revealed more or less stenosed, fleshy thickening at various parts of the intestinal wall, more marked in the terminal ileum and extending to the jejunum. There was no ulceration of the mucous membrane and no enlargement of the mesenteric lymph nodes. The operative specimen, which consisted of 15 cm. of the most stenosed segment of the terminal ileum, disclosed numerous sarcoid tubercules with a few giant cells, but there were no signs of necrosis. Confluent masses of sarcoid lesions were more frequent in the submucosal areas, but involvement of the muscular coat and of the subperitoneal coat were also seen.

The administration of cortisone was started 15 days after the operation in doses of 50 mg. daily for one month. The patient's postoperative improvement was slow and was probably aided by cortisone therapy. Her clinical cure has now been maintained for four years, and she leads a normal life. The authors do not share the opinion concerning correlation between tuberculosis and sarcoidosis, and believe that the rare condtion of sarcoidosis of the ileum should be differentiated from Crohn's regional ileitis as well as from tuberculosis.

Multiple Cancers in Colon Surgery: Report of 162 Cases. R. A. McGregor and H. E. Bacon. Surgery 44:828-833 (Nov.) 1958 [St. Louis].

Of 1,788 patients with microscopically verified cancer of the colon and the rectum who were admitted to the department of proctology of Temple University Medical Center between September, 1940, and May, 1958, 162 (9.1%) had multiple primary malignancies. There were 90 men and 72 women. Ninety-four of these 162 patients had multiple primary lesions of the large intestine alone, an incidence of 58.1% among the patients with multiple primary malignancy and an incidence of 5.3% among the total number of patients with cancer of the colon and rectum. The remaining 68 patients (41.9%) had involvement of large intestine and of organs or systems other than the colon. Of the 94 patients with multiple primary lesions of the large intestine alone, 60 were men and 34 were women. In addition to these 60 men, there were 9 men with second or third primary cancers in the upper gastrointestinal tract. Only 1 woman in the entire series had a second carcinoma involving the upper gastrointestinal tract. These data suggest that men show a definite predisposition to involvement of tions are potentially good candidates for chemopallidectomy provided definite progression of the disease, failure of medical therapy, and a marked degree of involvement justify this course of action. Most patients over 60 to 62 years of age, especially those in wheel chairs or bedridden with oversalivation or other symptoms listed above, should not be operated on in the present state of knowledge and experience. Almost all writers today agree that the ideal candidate for the operation is under 60 years of age, preferably with only one side grossly involved, with poor response to medication, still ambulatory and in good general condition, but with diminished earning power.

With these restrictions in the selection of patients, and with the meticulous use of either (1) the chemopallidectomy technique using alcohol, or (2) the McKinney's subcortical pallidotomy knife cutting procedure, good results can be obtained in approximately 60 to 70% of patients with Parkinsonism chosen for operation. Statistically, therefore, there is as much if not more justification for neurosurgical treatment of Parkinsonism as there is for neurosurgical treatment of intractable pain, focal epilepsy, and other diseases which merit the attention of neurosurgeons. The general practitioners, who care for the large population of Parkinsonism patients, should now consider neurosurgical intervention as one possibility in the treatment of selected patients with moderately advanced lesions. Neurologists can consider the fact that neurosurgery has produced satisfactory relief for 3 years or longer in many patients with Parkinsonism.

Gastric Ulcer: Survey of the Rhode Island Hospital Cases in the Ten-Year Period from 1946 through 1955. J. R. Bernardo, C. H. Soderberg and A. V. Migliaccio. Surgery 44:804-812 (Nov.) 1958 [St. Louis].

Of 519 patients with gastric ulcer who were admitted to the Rhode Island Hospital between 1946 and 1955, 142 were treated medically and 377 surgically. There were 364 male patients and 155 female patients between the ages of 10 and more than 81 years. Of the 364 male patients, 331 had benign ulcers and 33 had malignant ulcers; of the 155 female patients, 138 had benign ulcers and 17 had malignant ulcers. Duration of symptoms in the entire group of 519 patients averaged 4.7 years, as compared with an average duration of 1.3 years in the group with malignant ulcers. There was no difference in significant weight loss between the patients with benign and malignant ulcers. The incidence of massive hemorrhage was higher (11%) among the patients with benign ulcer than that (4%) among the patients with malignant ulcer. The presence of a duodenal ulcer does not rule out malignancy in an associated gastric ulcer, since 3 (6%) of the 50 patients with malignant ulcer had an associated duodenal ulcer. Multiple gastric ulcers were associated only with benign lesions.

Of the 469 patients with benign ulcer, 179 were tested for free acid and 25 (14%) of these showed absence of free acid; thus a significant number of patients with benign gastric ulcer had achlorhydria. Of the 30 patients with malignant ulcer who underwent this test, 12 (24%), however, had elevated acid values of 41 and more units. Therefore, the determination of free acid cannot be considered a reliable diagnostic tool. Gastroscopy has been unreliable in the authors' experience. Gastrointestinal roentgenographic examinations were performed on 301 of the 519 patients. Of 151 patients whose ulcer was considered benign roentgenographically 10 had malignant ulcers, the accuracy of the diagnosis being 93.8%. Of 36 patients with a roentgen diagnosis of malignant ulcer, a pathological diagnosis of malignant ulcer was made in 11 (23.4%). The overall x-ray accuracy on both benign and malignant lesions was 78%, which is only slightly lower than the 85 to 90% reported by other workers. With increasing size of a gastric ulcer the chance of its being malignant, increases as a rule, but the 5 largest ulcers, all over 6 cm. in diameter, were benign. Thus the size of the ulcer, although it is of some help in determining the presence of malignancy, cannot be taken as a reliable guide to the differential diagnosis of the individual lesion. Benign ulcers are more common in all areas of the stomach compared with the malignant ones. About 1 out of 5 lesions of the antrum, excluding the prepyloric area, was maligant. One out of 7 ulcers in the prepyloric area proved to be malignant.

Of the 142 patients treated medically, 17 (12%) died, including 12 dying from hemorrhage so severe as to prevent their being brought into condition for surgical treatment. Of the 377 patients treated surgically, 25 (6.6%) died. Subtotal gastrectomy was performed electively for gastric ulcer on 318 of the 377 patients; a high rate of minor complications (30%) and an operative mortality rate of 4.1% was noted.

Intervertebral Disc Removal and Spine Fusion. E. L. Compere, W. Schnute, C. L. Compere and R. G. Thompson. Am. J. Surg. 96:624-630 (Nov.) 1958 [New York].

Of 154 patients with herniated intervertebral disk lesions who were operated on by the authors between 1945 and 1952 and were subjected to spine fusions combined with surgical removal of the disk, 120 answered a questionnaire which was sent to them in an attempt to evaluate the end-results. Of these 120 patients who had been followed for periods of from 4 to 11 years, 83 were between the ages of 31 and 50 years, 17 were less than 30 years of age and 20 were between the ages of 50 and 70 years. Fifty-three patients (44.1%) had obtained excellent results, 32 (26.6%) good results, 21 (17.5%) satisfactory results, and 14 (11.8%) poor results. Only 21 (17%) of the 120 patients complained of residual back pain. Adding spine stabilization procedures to simple disk excision did not cause any increased incidence of morbidity in this series of patients as compared with those undergoing only a simple disk excision. The average duration of the patient's stay in the hospital was 18.4 days, which was not much longer than that of patients on whom only the simple procedure was performed. The results obtained were far from perfect but with increased attention to the finer details of spine fusion technique they can be improved. Although some of the patients exhibited a pseudarthrosis, these spines were remarkably stable due to dense fibrous tissue formation resulting in a decrease in back pain.

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It is evident that multiple primary malignancy, of the large intestine at least, is not a rare or even an unusual phenomenon. Any patient with a carcinoma of the rectum or the colon has an increased risk of cancer occurring at other sites, simultaneously or at different time intervals. The relative incidence of primary multiple cancer may be high or low according to the various reports by other workers, but the fact that it is a definite possibility is the important point. All physicians must be alert to this possibility and must abide by the following rules when a cancer patient is dealt with: 1. Preoperative investigations should include a careful physical examination, proctosigmoidoscopy, and roentgenologic examinations. In men, upper gastrointestinal roentgenograms are advisable. The slightest gastrointestinal symptom in women should warrant barium meal studies. 2. During surgical intervention meticulous exploration of the colon and of all abdominal organs should be performed. Coloscopy often reveals lesions missed by palpation. 3. After the operation patients should be checked at regular intervals, both clinically and roentgenographically. Each patient should remain on the cancer detection list because of the possibility that an additional primary cancer may occur even though the patient's survival time, whether it be 5, 10, or even 20 years, suggests theoretically a surgical cure.

Significance of Peroperative Cholangiography in the Management of Gallbladder Disease. P. A. Ykelenstam. A. M. A. Arch. Surg. 77:684-688 (Nov.) 1958 [Chicago].

The author reports on 20 men and 80 women, between the ages of 27 and 88 years, with gallbladder disease, who were operated on at the St. Canisius Hospital in Nijmegen, The Netherlands, and on whom cholangiography was routinely performed in the course of cholecystectomy. A comparison was made with a series of 100 patients in whom the gallbladder was removed without the aid of cholangiography in the course of the surgical intervention. Conventional indications for exploratory examination of the biliary system were present in 64 of the 100 patients operated on with the aid of cholangiography. Shadows were revealed by the cholangiography in 19 patients, and in 3 of them the shadows were suspected to be ascribable to air bubbles. Occlusion of the papilla of Vater appeared on roentgenographic evidence to be present in 10 patients and was confirmed by exploration in 8; in 16 patients the duodenum did not fill with contrast medium after a single injection; after a second injection no filling was observed in 12 patients. In 8 patients this appeared to be due to the presence of a calculus in the papilla. In the remaining 4 patients no pathological changes or calculi were found. In 15 of 37 patients with a history of jaundice, roentgenograms of the opacified area revealed shadows (probably caused by calculi); in the course of the ensuing choledochotomy stones were actually found.

The reported data suggest that unnecessary exploration of the bile ducts was prevented in 40 patients, so that drainage of the common bile duct could be avoided and, consequently, the risk of complications reduced and the time of hospitalization shortened. In 4 patients exploration did not yield any results, and in 3 of them the presence of air bubbles had been suspected previously. In 5 patients in whom no indications for choldochotomy appeared to be present, the cholangiogram revealed shadows caused by stones and, on exploration, stones were found. This experience alone would seem to be sufficient justification for the routine performance of contrast roentgenography during cholecystectomy. There were indications for exploration of the common bile duct in 56 of the 100 patients in the control series. Exploration was performed in 50 of the 56 patients, and in 23 of the 50 patients exploration proved to be unnecessary. The use of cholangiography in the course of surgical intervention is recommended in all operations performed on the basis of suspected gallstones or biliary obstruction, hypersensitivity to iodine or the patient's precarious condition being among the only reasons for abandoning this type of examination. With adequate technique and sufficient experience, cholangiography performed in the course of surgical intervention is considered a reliable diagnostic aid in establishing the presence of calculi in the bile ducts.

Metastasized Malignant Thymoma and Myasthenia Gravis. M. R. Poinsi, J. Chapin, H. Payan and G. Darcourt. Presse méd. 66:1506-1508 (Oct. 1) 1958 (In French) [Paris].

Malignant thymoma metastasizing to the liver was found to be the cause of death in a 24-year-old woman. Severe asthenia and loss of weight which had existed for three years had been attributed to over-exertion. Fluoroscopic examination revealed a shadow of doubtful significance in the middle mediastinum. The patient's condition gradually grew worse during the next two years; severe muscular disorders appeared, and she had difficulty in swallowing, in chewing, and in talking. Neurological examination revealed myasthenia gravis which was typical except for the fact that it could not be brought under control by the administration of prostigmin. Roentgenograms of the thorax made from the anteroposterior and lateral plane showed enlargement of the thymus. On abdominal palpation the outlines of the liver were found to be irregular and bosselated. Laparoscopy revealed a typical secondary neoplasia. The operative intervention undertaken for the purpose of removing the thymic tumor disclosed a large (10 cm. in vertical diameter, and 7 cm. in horizontal diameter) lobulated and woody thymus, which was inoperable, extending to the middle portion of the mediastinum on the right side. There was extensive metastasis to the liver, characterized by multiple nodules (varying in size from a hazelnut to that of an apricot) on the left lobe of the liver, and by a tumor involving almost completely the right lobe of the liver. There was no direct continuity between the liver and the thymic tumor.

A transient improvement was noted in the patient's condition after the exploratory thoracotomy, and for the period of two months the ingestion of from 7 to 8 tablets daily of prostigmin was sufficient to alleviate the symptoms. Her liver, however, gradually increased in size, severe motor disturbances involved the arms, and difficulty in breathing developed despite the administration of 27 tablets daily of prostigmin. The patient died of asphyxia five months after the operation. Histologic study of biopsy specimens taken from the liver and the thymic tumor revealed a mature thymic epithelioma of complex structure containing epithelial elements of different morphologic modifications, and small lymphocyte or thymocyte cells.

A review of the literature shows that malignant tumors of the thymus in patients with myasthenia gravis are unusual, but the occurrence of metastasis to the liver is still more exceptional.

GYNECOLOGY & OBSTETRICS

Pathology and Treatment of Mammary-Duct Fistula. D. H. Patey and A. C. Thackray. Lancet 2: 871-873 (Oct. 25) 1958 [London].

The authors report on 7 women, between the ages of 24 and 48 years, with a fistula of a large mammary duct near the nipple who were operated on at the Middlesex Hospital in London. The youngest patient had had no children and the oldest had had 2. The condition was associated with some degree of retraction of the nipple in 6 of the 7 patients. The typical history was that of the occurrence of a lump eccentrically situated under the areola, sometimes but not always with the clinical features of an abscess. The abscess either ruptured or was opened and drained, but did not permanently heal. Periods of apparent healing alternated with periods of discharge from a small granulating orifice situated at the margin of the areola. The fistulas were excised completely up to the opening of the involved duct at the nipple. The operative specimens were studied pathologically. Microscopic examination revealed that the condition is associated with a duct lined with squamous epithelium, in contradistinction to the normal lactiferous ducts which are lined by 2 layers of cells, the inner columnar epithelium and the outer flattened myoephithelium. In 2 specimens, the presence of sebaceous glands opening into the abnormal duct pointed to a congenital abnormality. In others, the abnormal lining of the duct may result from squamous metaplasia; there is, however, evidence against this view and all cases may represent a congenital abnormality.

Mammary-duct fistula is a common cause of persistent or recurrent inflammation and discharge after a periareolar abscess. The rational radical treatment is complete excision of the fistula and the abnormal duct; if exteriorization proves in practice to be equally satisfactory, it may be preferable as interfering less with the normal ducts of the nipple.

Cancer of the Breast: A Study of Short Survival in Early Cases and of Long Survival in Advanced Cases. D. W. Smithers. Am. J. Roentgenol. 80:740-758 (Nov.) 1958 [Springfield, Ill.].

The author reports on 2,648 patients with cancer of the breast seen at the Royal Marsden Hospital in London, England, between the years 1937 and 1953. In 583 (22.0%) of these patients the tumor was in stage I and 38 (7.0%) of these died within 2 years of treatment. At the time of death they had distant blood-borne metastases with a predominance of those in the liver and the brain. The grade of tumor had been recorded in 19 of the 38 patients. Three of those had grade I tumors, 8 had grade II and 8 other patients had grade III tumors. Eleven patients had tumors of the inner half of the breast. Treatment by surgery and irradiation gives excellent results as long as the disease is still well localized, but these methods fail if blood-stream dissemination has occurred. The factors of chief importance in judging direction of spread and in estimating the chance of dissemination in clinically early cases are the grade and size of the tumor, the length of history, the site of the tumor, and the age of the patient. Standard treatment applied rigidly according to the stage alone represents a denial of clinical judgment. Unfavorable prognosis should limit the use of surgical methods, which may make matters worse if a complete success is not warranted. Large medial tumors in stage I with a short history are, however, the only ones in which irradiation before mastectomy is often indicated especially when the patient is obese and difficult to examine. The prognosis is comparatively bad for patients with tumors in the early stages located in the inner half of the breast in contrast to those in the outer half of the breast. This is due to the fact that tumors of the inner half of the breast lead to more frequent involvement of the clinically less easily detectable parasternal lymph nodes. Thus patients with tumors of the inner half of the breast in an early stage require special care in treatment, and the question of preference for surgery or irradiation in the less malignant grades is still undecided. Older women tend to wait longer before coming for treatment and have therefore a more unfavorable stage distribution than younger women, but age also affects the prognosis in the young in as much as hormonal influences are concerned. Tumors developing during pregnancy or lactation have a relatively bad prognosis whereas those developing shortly before the menopause may have a relatively good one. In all young women before the menopause who have grade III tumors, multicentric origin, extensive perivascular or perineural lymphatic permeation or involvement of axillary fat, an artificial menopause should be considered as part of the first planned treatment.

Another study in 293 patients with cancer of the breast, stage IV, admitted to the same hospital between 1940 to 1949 showed that 2 patients survived 3 years or more; 9 of these were premenopausal and 12 postmenopausal by more than 10 years. There were no 3 year survivors among the patients in stage IV who were treated within 10 years after the menopause. In 7 of the 9 patients in the premenopausal group, menopause was induced and initial roentgenotherapy was given. Three of the 7 patients were still alive 13, 10 and 9 years afterwards (2 with no further treatment other than the initial roentgenotherapy and induced menopause; 1 at 10 years after the whole therapeutic gamut of oophorectomy, adrenalectomy, testosterone injections, and further irradiation). The remaining 2 of the 9 patients were treated with estrogens at the time of their initial roentgenotherapy. Eight of the 12 postmenopausal patients who survived 3 years or more were given estrogens, all had roentgenotherapy and 1 had in addition local mastectomy.

These data show that although early breast cancer is regularly curable, some patients may nevertheless die within a short time in the course of the treatment. The invasiveness and danger to life once advanced breast cancer has reached this stage cannot well be denied, but estrogen treatment combined with irradiation may give some long-term survivals.

The Histogenesis of Ovarian Tumours. R. E. Rewell. J. Obst. & Gynaec. Brit. Emp. 65:718-726 (Oct.) 1958 [London].

The author reviews observations on several hundred ovarian tumors seen chiefly in one center in England and in one in India. A table lists the diagnoses in 209 patients at the Women's Hospital, Liverpool, England, and in 118 patients at the Government Hospital for Women and Children, Madras, India. The author saw relatively more rare tumors than are listed in the table, because specimens of doubtful and interesting tumors were often sent to him from other institutions, so that he estimates that he studied approximately 500 ovarian tumors. He found that adenocarcinoma was relatively more frequent in India than in England, there being 37 adenocarcinomas among 118 ovarian tumors studied in Madras and only 34 among 209 in Liverpool.

He found that the boundaries between many of the accepted types of ovarian tumors are much less clear than is usually realized, e. g., the granulosa-cell and thecal-cell tumor form a continuous series, nor can some Brenner tumors be divided from them sharply, while these again merge into some types of pseudomucinous cystadenoma. These tumors form a group by themselves, what may be termed the "stroma-follicle" group and they are best regarded as derived from the common stem of theca and follicle cells in the normal adult ovary at quite a late stage in their differentiation. Among these tumors structural differentiation by no means runs parallel with functional differentiation and vice versa. The series confirmed previous observations that the appearance of the Brenner tumor, and possibly that of the pseudomucinous cystadenoma, is nonspecific and may be produced by different modes of development, nor are these in themselves of a uniform pattern. The terms "granulosa-cell," "thecal-cell," and "Brenner" applied to tumors are of clinical convenience only. These terms must not be thought of as excluding a common origin for the group, while many individual tumors fall into areas of overlap between them even when used in a purely descriptive sense.

Teratomas are probably derived from a distinct stem of primitive cells, as also are dysgerminomas and probably arrhenoblastomas. Routine study of ovaries removed at operation confirms modern theories of the close relationship of stromal and follicle cells and tends to support the possibility of the origin of new follicles in the adult ovary.

Fetal Electrocardiography, with Special Reference to Early Pregnancy. S. D. Larks and K. Dasgupta. Am. Heart J. 56:701-714 (Nov.) 1958 [St. Louis].

The authors recorded 260 fetal electrocardiograms which were obtained from 145 pregnant women. In certain of these women as many as 16 consecutive recordings were obtained through the full gestational period. Between the 16th and 22nd weeks of pregnancy the fetal electrocardiograms became large, sharp, and clear. At this time and afterward the fetal electrocardiogram may become of diagnostic importance. The earliest fetal complexes were recorded in this series, at 11½ to 15 weeks; they were directed downward. Judging by the consistent relationship which was observed between such complexes and breech presentations at later stages of gestation when clinical or roentgenographic evidence was available, it would seem that, ordinarily, the fetus presents by the breech at this early period of pregnancy. Similarly, the fact that the fetal-QRS changed to an upright complex in the usual case at about 20 weeks suggested that rotation to the more common vertex presentation takes place at about this time. It is possible that a combination of rotation about 2 axes, not only the transverse but also the longitudinal axis of the fetus, might make changes in the fetal electrocardiogram which could resemble breech-to-vertex rotation. The fetal electrocardiogram thus provides rapid information as to the presence of a living fetus, and its presentation.

Recordings from 4 sets of twins are presented which indicate the value of fetal electrocardiography in cases of multiple pregnancy. A diagnosis of multiple pregnancy was made at 21 weeks in a pregnant woman from whom tracings were obtained as follows: the first at 16 weeks, and the second, third, and fourth tracings at 21 weeks. This electrocardiographic diagnosis was immediately confirmed roentgenographically. Actually, it is possible to make the diagnosis from the tracing of the 16th week. In other cases, recordings of the fetal electrocardiogram in utero, and subsequent electrocardiograms of the newborn infant were obtained for both vertex and breech presentations. The identity of the complexes was beyond doubt. The presence of a cardiac anomaly in the fetus was revealed in another case at the 20th week of gestation by several unusual features in the electrocardiographic tracing. The direction of the complex seemed to indicate a vertex presentation, yet roentgenographic evidence showed a breech. The complexes were unusually wide and notched, suggesting conduction difficulties. The complexes showed the prolonged overshooting which cardiologists usually refer to as S-T segment displacement. In this case the infant showed delayed respiration at delivery and survived only 5 days. At autopsy, coarctation of the aorta was observed. Utilizing presently available instruments and techniques fetal electrocardiograms thus can be recorded in utero even early in pregnancy and may be a valuable diagnostic aid in obstetrics and allied fields. In general, fetal electrocardiography provides positive results from 2 to 6 weeks before the first auscultation of the fetal heart tones.

Recurrent Pregnancy Toxaemia. D. W. S. Gordon and M. R. Fell. J. Obst. & Gynaec. Brit. Emp. 65: 727-733 (Oct.) 1958 [London].

That toxemia of pregnancy does tend to recur has been known for many years, but little work has been done on this problem, and so it was decided to assess, as accurately as possible, exactly what is the chance of pre-eclamptic toxemia recurring. The theory that a renal lesion was the factor behind the recurrence has now been discarded. However, the possibility that these women were getting toxemia again because of an inherent tendency to develop essential hypertension has gained some support and, as a corollary to the main problem, it was decided to see if there was any evidence to substantiate this theory. Finally, an analysis was made of 3 factors which it seemed might influence the chance of recurrence—namely, the severity of the initial toxemia, its duration, and time of onset in pregnancy. The 996 cases of toxemia which occurred at a maternity hospital during a period of 5 years, when 17,562 deliveries were made, form the basis of this report. The criterion for toxemia was a blood pressure of 140/90 or over, together with the presence of albuminuria and/or definite edema. The combination of hypertension and edema without albuminuria was very unusual.

In commenting on their findings the authors state that the chance of any woman who has had pre-eclamptic toxemia developing it again in her next pregnancy is 45%. If pre-eclamptic toxemia occurs in 2 consecutive pregnancies the risk of a further recurrence rises to 72%. Should it occur 3 times running, then toxemia a fourth time is almost a certainty. If a woman who has had pre-eclamptic toxemia does not develop it again in her next pregnancy then the risk of her ever developing it again in subsequent pregnancies is only 6%. Pre-eclamptic toxemia developing in association with multiple pregnancy behaves differently and merits consideration as a separate problem. Thus there were 10 women with twins, in all of whom signs of pre-eclamptic toxemia developed for the first time during the twin pregnancy, but it developed in none of these women during the subsequent pregnancy. It may be that toxemia associated with multiple pregnancy does not carry the same risk of recurrence in future pregnancies as does toxemia occurring with a single pregnancy.

Patients classified as having a severe form of pre-eclamptic toxemia appeared to have a higher chance of recurrence. However, it cannot be claimed that severity itself is the deciding cause. Eclampsia carries less risk of recurrence than toxemia without fits. The length of time the toxemic process is active may have some bearing on this point, if, as is often the case, eclamptic fits supervene on a fulminating type of pre-eclamptic toxemia, so that although this is toxemia in its most severe form, the whole process is relatively short-lived. In this connection it is pointed out that with the present-day trend toward early induction of labor, the duration of the process in relation to recurrence is of doubtful significance. No evidence was found on analyzing subsequent blood pressure levels to suggest that these women were developing recurrent toxemia because of the associated onset of essential hypertension. The time of onset of the toxemic process is of doubtful significance especially as a higher proportion of the "severe" cases occurred in the earlier onset group. This survey was conducted by a retrospective investigation and has all the disadvantages associated with this. There are many other factors that could be investigated.

The Determination of the Genetic Sex. G. Sansone and A. Tomassetti Levi. Minerva pediat. 10:925-932 (Sept. 22) 1958 (In Italian) [Turin, Italy].

The genetic sex according to the leukocyte morphology test devised by Davidson-Smith was investigated in 3 groups of persons. The test conducted by each author independently from each other indicated the correct genetic sex in one group of 300 children and adults with normal sexual features. The sex identity was not disclosed to the investigators until after the diagnosis was made. The number of drumsticks was larger in the younger than in the older individuals.

The second group consisted of 67 newborn infants, 36 being premature and 31 born at term. The percentage of drumsticks in the immature female newborn infants was on average 8.3% with variation from 3 to 15%. The percentage of drumsticks in mature female newborns was on average 7.5% with variation from 2.8% to 16%. Ten pairs of female dichorial and enzygotic twins were included in this group. The small number of newborn infants in this group did not permit one to draw any conclusion. The third group consisted of 16 persons, aged between 1 month and 21 years, with gonadal dysgenesis, 14 of whom had the Bonnevie-Ullrich syndrome and 2 had the ovarian agenesis. The test was repeated several times. Sex chromatin test was negative (male) in 10 of these patients and positive (female) in 4. Examination of the smears from the oral mucosa suggested a chromatin-negative response in 1 patient in whom the response to Davidson-Smith test was equivocal. The sex chromatin test in 2 patients with ovarian agenesis suggested masculine genetic sex. The determination of the genetic sex by Davidson-Smith technique in the third group was significant, because most of the patients passed the puberal age and did not show any secondary sexual features nor had they menstruated.

PEDIATRICS

Pancreatitis in Young Children. J. Collins. Arch. Dis. Childhood 33:432-436 (Oct.) 1958 [London].

Pancreatitis is rare in young children. The author describes the pathologic changes found in the pancreas at autopsy in 4 children, all aged 2 years or less. Three of the children concerned were Bantu of N. Rhodesia and were the only ones found to have pancreatitis in the routine examination of material from 100 consecutive autopsies on African children. The fourth child, included for comparison, was an Edinburgh girl and the only case of pancreatitis in the records of 1,812 consecutive postmortem examinations. In each of these children inspissated secretions had caused the dilatation, obstruction, and subsequent rupture of intralobular ducts, and in two cases the resulting pancreatitis had been confined to a very small area and was undergoing healing by fibrosis. It is suggested that this inspissation is brought about by a combination of vagal stimulation, dehydration, and the absence of normal pancreatic secretions over a period of time probably measured in days. If this theory of the cause of these intraductal obstructions is correct then, apart from the normal procedures to remedy dehydration, other measures to overcome vagal stimulation (where this is present) and to encourage normal pancreatic secretions are indicated in all very young sick children.

A Test for Coeliac Disease. W. W. Payne and V. Jenkinson. Arch. Dis. Childhood 33:413-416 (Oct.) 1958 [London].

The relationship between wheat flour in the diet and the development of symptoms in children with celiac disease observed by Dicke in 1950 has been established. Subsequent investigations indicated that the injurious factor occurs principally in the gliadin fraction. Weijers and van de Kamer in 1955 used gliadin for testing, hoping that the test would be helpful in the diagnosis of celiac disease. In order to determine the value of this gliadin tolerance test, the authors performed it on a series of children with celiac disease and on controls. Thirty-three patients with celiac disease were studied. The diagnosis was made according to stated criteria in 25, and in 8 it was based on clinical data associated with the response to a gluten-free diet, and relevant biochemical investigations were not made. Two of the children were in the active phase of the disease in that treatment had not been instituted when they were tested. Eight children had been on a gluten-free diet for periods of a few days to one month before their gliadin tolerance test. These children have since shown a satisfactory response to the therapeutic diet. The rest of the patients had been treated for some years, having had periods on a gluten-free diet and on a normal diet. Some children, who had been treated for more than 4 years, still deteriorated when returned to a normal diet. A few patients had apparently recovered after prolonged treatment; they had shown no recurrence of symptoms when returned to a normal diet and growth continued at the expected rate. Six children in this series were either undiagnosed or untreated for a long time after the onset of symptoms.

Contratest cases were selected from convalescent patients who had had diseases with no alimentary tract involvement, with the exception of one child, who was a normal healthy unlike twin of one of the patients with celiac disease. Four children who were convalescent from disorders of the alimentary tract from causes other than celiac disease formed a second contratest group. Gliadin was prepared according to the procedure recommended by van de Kamer. The authors found that the increase of apparent plasma glutamine after a test dose of gliadin was significantly greater in children with celiac disease than in contratest children. Children convalescent from gastrointestinal dysfunction from causes other than celiac disease showed an increase intermediate between healthy children and those with celiac disease. There was no quantitative relation between increase of plasma glutamine and phase of the disease, whether acute or nonsymptomatic through withdrawal of wheat and rye gluten from the diet. Diet appeared to have no influence on the degree of increase of plasma glutamine. The overlap of range of results from contratest subjects and celiac disease patients is considerable and does not recommend the test as a diagnostic one.

OTOLARYNGOLOGY

Cytologic Diagnosis in Otorrhinolaryngologic Neoplasms. T. Ferreira Lorenzi. Rev. Hosp. clin. 13: 291-296 (July-Aug.) 1958 (In Portuguese) [São Paulo].

The cytologic diagnosis of otorrhinolaryngologic cancer is based on the aspect of the tumor cells and the character of the structures which form the cells. The cells are atypical. They are arranged in abnormal groups. The nuclei present abnormalities of size, number, limits, contents of chromatin, mitoses, and nucleoli. As a rule the nuclei are much larger than those of normal cells. The cytoplasm is scanty and the nucleus-cytoplasm ratio is increased. Seventy patients with malignant otorrhinolaryngologic tumors were observed at the Clinica Otorrinolaringologica of the Hospital das Clinicas of the University of São Paulo. Cancer was located in the nose (13 cases), the maxilla (9), the mouth (22), the nasopharynx (4), the larynx (9), the neck (9), and other otorrhinolaryngologic structures (4). A cytologic diagnosis was made by the Papanicolaou and Leishman's methods of stained smears. The smears were prepared with material obtained by scraping of the tumor, puncture, surgical biopsy and scraping of surgical specimens. The cytologic diagnosis was positive for cancer in 66 out of 70 patients. There were 3 false positive results in the smears prepared with material from the mouth of a patient with Southamerican blastomycosis, the larynx of a patient with laryngeal tuberculous ulceration and from the material obtained by puncture of an enlarged cervical lymph node in a patient with scrofula. The only false negative result was on a smear prepared with material from a mixed tumor of the parotid gland with carcinomatous degeneration. The author concludes that the cytologic diagnosis by the Papanicolaou and Leishman's methods is of value in the diagnosis of cancer of the mouth, pharynx, larynx, and other otolaryngologic structures. It is indicated in patients with clinical symptoms of otorrhinolaryngeal cancer when the results of histologic examination are negative. It is also of value in a differential diagnosis between oropharyngeal carcinoma and blastomycosis.

THERAPEUTICS

The Use of Raubasine in the Treatment of Angina Pectoris and of Cerebral Atherosclerosis. J. Pieri, M. Wahl, and J. Casalonga. Presse méd. 66:1523-1525 (Oct. 4) 1958 (In French) [Paris].

Raubasine, one of the alkaloids from Rauwolfia serpentina, is a pure sympatholytic agent capable of reversing the action of adrenalin and noradrenalin. It is essentially an arterial vasodilator with a gradual and persistent spasmolytic action. Lessening in both severity and frequency of anginal crises was pronounced in ⅓ and light in ½ of a group of 50 patients with angina pectoris who were treated with raubasine. Three mg. per day for 6 to 8 weeks benefited both patients with functional angina and those with confirmed coronary disease. Small doses bring a therapeutic improvement which probably lasts over a longer period of time than larger doses would produce. In 23 cases of confirmed ischemia of the myocardium, 7 were greatly improved, as much functionally as electrocardiographically, and 6 showed clinical improvement of the myocardium. Most of these patients had particularly tenacious and severe myocardial disorders of early appearance. Electrocardiographic improvement was in the modifications that seemed to be related to arterial spasm. Long duration of anginal disease is not a contraindication of raubasine. Raubasine associated with the total alkaloids of rauwolfia and with cardiac stimulants was given to patients with tachycardia and hypertension to treat the first symptoms of overloading of the myocardium. The advantages sought were (1) a neurosedative and bradycardiac action to complete the effect of mild cardiac stimulants, (2) a direct influence by raubasine on the circulation in the heart muscle, and (3) a diminution of the doses of total hypotensor alklaloids through the reinforcement exerted by raubasine. Of 22 patients with tachycardia and hypertension who were treated, only one developed symptoms of asystole.

Raubasine was used to treat the sequelae of various cerebrovascular attacks, the quality of results being in proportion to the precocity of treatment. Treatment with 3 to 5 mg. of raubasine coincided with disappearance of paresis of central origin or of motor awkwardness which were not accompanied by the Babinski sign in a little more than one half of the patients recently afflicted with clinical symptoms of cerebral ischemia. Treatment with raubasine is also effective in patients whose symptoms are more functional than organic, and are of long duration. Difficulties of equilibrium, vertigo, and persistent headache either disappeared or were strongly attenuated after doses of 3 mg. of raubasine for 1½ months in one third of 22 elderly patients with hemiplegia who were afflicted with various manifestations of atherosclerosis. Raubasine exerts a curative and possibly preventive action upon ischemic apoplectic attacks. It seems to gradually improve the circulation of blood in the myocardium and its results are not definite before 6 to 8 weeks of treatment. In this study it was well tolerated, had no side-effects, and provided encouraging results considering the usual severity of the conditions treated.

Fecal Enema as an Adjunct in the Treatment of Pseudomembranous Enterocolitis. B. Eiseman, W. Silen, G. S. Bascom and A. J. Kauvar. Surgery 44:854-859 (Nov.) 1958 [St. Louis].

The authors report on 3 men, between the ages of 46 and 68 years, and 1 45-year-old woman with pseudomembranous enterocolitis to whom retention enemas composed of normal feces suspended in sodium chloride solution were administered in an attempt to re-establish the normal intestinal bacterial flora. Cultures of the stool of all 4 patients had revealed Staphylococcus pyogenes var. aureus before this therapy was instituted. The latter is based on the fact that staphylococcic overgrowth occurs when other organisms disappear and that reintroduction of the bacteria, viruses, and bacteriophage normally found in the colon might re-establish the balance of flora with subsidence of staphylococcic predominance and the distressing symptoms caused thereby. In each of the patients, the clinical course was markedly improved and the Staphylococcus pyogenes var. aureus which grew in pure culture before the treatment disappeared from the stools and was replaced with normal colonic nonpathogenic agents after this therapy.

Attempts to produce in 2 dogs a progressive enteritis or bloody diarrhea within a previously sterilized isolated intestinal segment by the instillation of a pure broth culture of tetracycline-resistant Staphylococcus pyogenes var. aureus daily for 4 days failed. Thus it has not been possible to evaluate the fecal enema under controlled conditions. It is suggested that this simple yet rational therapeutic method should be given more extensive clinical evaluation.

PATHOLOGY

Splenoportal Occlusion in Patients Without Enlarged Spleen. G. Sotgiu, C. Cacciari, and E. Pisi. Minerva med. 49:3247-3251 (Aug. 29) 1958 (In Italian) [Turin, Italy].

The authors report on 60 patients with occlusion of the splenoportal veins, 52 of whom had enlarged spleen. Splenoportal occlusion associated with the enlarged spleen was present in 6 patients with a nonneoplastic disease and in 6 patients with a neoplastic disease of either the pancreas, biliary duct, or stomach. Of 8 patients without enlarged spleen, 6 had neoplasm, 1 had portal thrombosis accompanying calculous cholangitis, and 1 had splenic thrombosis accompanying cirrhosis. The authors suggest that the occlusion of the splenic vein is associated with an enlarged spleen mostly in those instances where the spleen is affected by an inflammatory or an infective process, such as in thrombophlebitic disorders. Splenoportal occlusions apparently do not cause the enlargement of a normal spleen, that is one which is not directly involved in a pathological process. The preceding 6 patients without enlarged spleen and a neoplastic disease of another organ illustrate this point. In the opinion of the authors the spleen did not enlarge in these patients because it remained intact. It is possible that a diminished arterial flow adjusted itself gradually to a diminished venous flow and thus did not produce the enlargement of the spleen.

The Experimental Production of Atherosclerosis in Swine Following the Feeding of Butter and Margarine. H. C. Rowsell, H. G. Downie and J. F. Mustard. Canad. M. A. J. 79:647-654 (Oct. 15) 1958 [Toronto].

The authors studied the changes in blood lipids and blood coagulation and the development of atherosclerosis in 33 swine, divided into 3 groups, fed either a low-fat diet or isocaloric diets rich in butter or margarine. Some atherosclerosis was observed in swine on a low-fat diet. The high-fat diet containing margarine as the fat source caused little increase in the amount of atherosclerosis, while a high-fat diet containing butter produced a considerable increase in the amount of atherosclerosis. There was no increase in blood cholesterol and phospholipid levels in the swine on the butter or margarine diets. The coagulation indexes studied at the completion of the experiment were most active in the butter-fed swine with the most considerable atherosclerosis. The course of the disease and the gross and microscopic findings of atheroma resembled those found in man. The evidence from this study suggests that the activity of the clotting system is related to the development of atherosclerosis in swine, and the type of fat fed is an important factor in determining these changes.

Endocardial Fibroelastosis: A Summary of the Literature and a Review of 24 New Cases. W. F. McCormick. South. M. J. 51:1232-1240 (Oct.) 1958 [Birmingham, Ala.].

Of 11,347 autopsies performed at the institute of pathology of the University of Tennessee College of Medicine and at the Baptist Memorial Hospital in Memphis between 1947 and 1957, a diagnosis of endocardial fibroelastosis was made in 24. This represents an incidence of about 0.2% of all the autopsies. There were 15 cases in which no other lesion was found in the heart, and these were classified as primary. The remaining 9 cases occurred in association with such congenital cardiovascular defects as interventricular septal defect (4 cases), patent ductus arteriosus (1 case), patent foramen ovale (3 cases), and infantile coarctation of the aorta (2 cases). These 9 cases were classified as secondary. Of the 24 patients with endocardial fibroelastosis, 13 were males and 11 were females, substantiating the findings of other workers that there is no real sex difference. There were 16 white and 8 Negro patients. Since the percentage of Negro patients in the total autopsy population outnumbered the white, this difference may be a real one, although most other workers did not find any racial difference. The average age of the patients with primary endocardial fibroelastosis was 10 months, and that of those with the secondary condition was 14 months. These figures are in agreement with those found in the literature.

Cyanosis was observed in 7 of the 15 patients with primary endocardial fibroelastosis but in only 3 of the 9 with the secondary condition. Murmurs were heard in only 2 of the 15 patients, and in 7 of the 9 patients. The absence of murmurs in the primary form seems to be of real value in the clinical diagnosis. Murmurs found in the secondary form are undoubtedly due, in most of these patients, to the other anomaly present, such as a septal defect. Cardiac hypertrophy was a constant feature in both groups. This enlargement was often extreme, with hearts found up to 5 times their normal size. A clinical diagnosis of primary endocardial fibroelastosis was made in 2 patients, and a pericardial poudrage with U.S.P. talc was done. Both of these patients lived only a short time. A clinical impression of endocardial fibroelastosis was correct in 2 other patients with the primary form of the condition. A third patient who had the secondary form of the condition underwent surgical correction for the associated interventricular septal defect and died on the second postoperative day.

The gross anatomic findings in primary endocardial fibroelastosis were remarkably constant. Cardiac hypertrophy was always present. The left ventricle was involved in almost all the patients, often without involvement of any other chamber. The endocardium was grossly thickened, often measuring 1 to 3 mm. in thickness. The heart valves were involved infrequently in this series, but other workers have reported involvement in about 50% of all the patients. Unlike some of the reports in the literature, secondary endocardial fibroelastosis was not seen in most cases of congenital heart disease in this autopsy population. This may be due to a more rigid selection of cases on the part of the author. Only those cases with significant gross evidence of endocardial thickening were used in this study. Microscopically, the absence of increased glycogen in the myocardium was a constant finding. The chief finding was thickening of the endocardium. It has been suggested that this thickening is due to deposition of fibrin from the blood and gradual incorporation of this fibrin into the endocardium. The evidence for this, based chiefly on electromicroscopic observations, is inconclusive at this time. Attempts by the author and by other workers to stain fibrin selectively have failed.

RADIOLOGY

Visualization of the Coronary Circulation by Occlusion Aortography: A Practical Method. C. T. Dotter and L. H. Frische. Radiology 71:502-524 (Oct.) 1958 [Syracuse, N. Y.].

The authors describe a technique for coronary angiography, which proved safe and reliable in dogs. The new technique of coronary arteriography is an occlusion aortography, which makes use of a special double-lumen balloon catheter to inject a small quantity of contrast agent (Thorotrast) close to the orifices of the coronary arteries during brief but total occlusion of the aorta just peripheral to the injection site. Since all the contrast agent enters the coronary arteries, maximum efficiency is achieved. Experimental observations during more than 500 complete aortic occlusions and 350 injections in 51 dogs support the belief that this technique is safe and reliable.

The increased efficiency of occlusion aortography for coronary visualization allows the use of small volumes of relatively dilute agents in obtaining improved visualization routinely instead of sporadically. By comparison, thoracic aortography constitutes a less efficient and more hazardous method for coronary visualization in that it involves the relatively uncontrolled intra-aortic injection of 10 to 20 times the needed amount of a type of contrast substance which has caused over 200 reported fatalities. The use of occlusion catheters in gaining controlled access to the cardiovascular system promises to open up many unexplored clinical and experimental possibilities, examples of which are (*a*) new techniques for cardiovascular visualization, (*b*) elective controlled cardiac arrest in the intact subject for purposes such as cardiovascular visualization, and (*c*) total cardiopulmonary bypass as an emergency therapeutic measure in the intact patient.

PUBLIC HEALTH

Report of an Outbreak of Febrile Illness with Pharyngeal Lesions and Exanthem: Toronto, Summer 1957—Isolation of Group A Coxsackie Virus. C. R. Robinson, F. W. Doane and A. J. Rhodes. Canad. M. A. J. 79:615-621 (Oct. 15) 1958 [Toronto].

The authors report on 47 children, between the ages of less than 6 months and 9 years, and on 13 adults, of an average age of 31 years, who were affected by a febrile illness with pharyngeal lesions and a vesicular rash in a suburb of Toronto in June and July, 1957. The distinctive triad of fever, ulcerative lesions of the fauces and the mouth, and a bullous eruption arising from a macular rash is considered to constitute a new clinical syndrome. The disease was mild in each of the 60 patients, and admission to hospital was not necessary. There were no sequelae. A total of 27 families was affected. Clinical disease occurred in 60 (52%) of the 115 members of these families. The illness spread progressively through adjacent blocks of houses and also from one family to another. The incidence of illness was highest in children of the 1-to-9-year age group (42 of the 47 children), and it was considered that they introduced the illness into the family groups. The high incidence of illness in this age group is explained by reason of the close contact of the children at play and in particular through use of small portable swimming pools.

Attempts at virus isolation were made by the inoculation of specimens obtained from 31 patients into monkey kidney-tissue and into suckling mice; virus was isolated from 22 of these patients (71%). The virus showed some serologic relationship to Coxsackie virus, group A, type 16. The isolation of this virus from 22 (79%) of 27 stool specimens obtained from these patients suggested a causal relationship between it and the clinical illness described. This suggestion was supported by the demonstration of a specific antibody response to the related Coxsackie virus, group A, type 16, in 3 patients, by the temporal relationship of virus isolation to the clinical syndrome in one patient, and by the absence of illness or virus isolation elsewhere in the population of the city of Toronto at the time of the outbreak and during the summer of 1957.

Observations on the Excretion of Type 1 Poliovirus from Cases and Their Contacts. L. A. Hatch, K. E. A. Hughes and J. N. Pilfold. Am. J. M. Sc. 236:419-424 (Oct.) 1958 [Philadelphia].

Many views on the application of quarantine measures for the prevention of poliomyelitis have been based on the recommendation of the World Health Organization (1954): "Children with familial or intimate exposure should be confined to their homes for 21 days. Adults need not be confined, but they should refrain from association with children other than their own and should avoid intimate contact with adults." Other workers described findings at variance with this recommendation. The authors report that at the Public Health Laboratory in Portsmouth, England, isolation of poliomyelitis virus was attempted in feces and throat swabs obtained from poliomyelitis patients and their contacts. This material was tested in HeLa cells. When the virus was isolated from feces, its identity was established by neutralization tests with monospecific hyperimmune monkey serums prepared from each of the 3 types of poliomyelitis virus. In many instances it was possible to examine repeated specimens of feces, collected at approximately weekly intervals. From July, 1956, until the end of 1957, type 1 poliomyelitis virus was isolated from 2 or more specimens of feces from each of 93 patients who were considered clinically to have nonparalytic or paralytic poliomyelitis, and also from 97 healthy contacts. From the results obtained it appears that half of the patients with poliomyelitis would be expected to excrete virus for about 3 weeks after the onset of their illness and that only after 8 weeks would this proportion fall to less than 10%. Half of the healthy contacts can be expected to excrete virus for about 5 weeks after the onset of illness in the index case, and the proportion would not fall below 10% until 8 to 10 weeks have elapsed.

These findings suggest that the rate of clearance of poliomyelitis virus from the stools follows an exponential curve. HeLa cells are generally regarded as being slightly less sensitive than other tissue cells in the detection of poliomyelitis virus in feces, and it may well be that these figures understate the length of period of excretion of poliomyelitis virus. This small series, however, indicates that the potential dangers arising out of the presence of poliomyelitis virus in the stools of a large proportion of convalescent patients and home contacts may persist longer than is generally recognized, though, in the absence of information on the amount of virus excreted, it would be unjustifiable to assume that the danger remains the same throughout the period of excretion.

BOOK REVIEWS

The Acute Abdomen. By William Requarth, M.D., Clinical Assistant Professor of Surgery, University of Illinois College of Medicine, Chicago. Foreword by Warren H. Cole, M.D. [Formerly titled Diagnosis of Acute Abdominal Pain.] Second edition. Cloth. $6.50. Pp. 313, with 89 illustrations. Year Book Publishers, Inc., 200 E. Illinois St., Chicago 11, 1958.

This book is designed primarily to assist young surgeons and medical students in the diagnostic problems that acute disorders of the abdomen may entail. It is proper then that detailed instructions relative to the examination of the abdomen be included. The value of the history as it relates to the patient's abdominal complaint is emphasized. It is in this area in particular that the depth of the author's experience becomes evident. Much of the clinical symptomatology has been tabulated to compare the merits of various signs and symptoms in relation to different abdominal diseases. Intestinal obstruction and its causes, diagnosis, and treatment, is thoroughly discussed, and excellent illustrations are presented. The latter half of the book gives the details of those diseases in which immediate operation is required, those in which operation can be delayed, and those in which it is contraindicated. In addition, traumatic wounds of the abdomen, congenital disorders, and the management of gastrointestinal hemorrhage constitute separate chapters. The principal assets of this book are its concise presentation and its small size. Its chief usefulness should be in emergency wards and surgical floors—wherever students, interns, and residents are in training. It should also be of benefit to physicians in general practice.

Roentgen-Diagnostics: Progress Volume I. By H. R. Schinz, R. Glauner, and E. Uehlinger. With collaboration of W. E. Beansch and others. Translated from German by James T. Case, M.D., D.M.R.E. [Rontgendiagnostik Ergebnisse 1952-1956, published by Georg Thieme Verlag.] Cloth. $35. Pp. 623, with 545 illustrations. Grune & Stratton, Inc., 381 Fourth Ave., New York 16; 99 Great Russell St., London, W. C. 1, England, 1958.

This magnificently printed, beautifully illustrated volume may be considered a companion to the previously published four-volume "Roentgen Diagnostics," by Schinz and co-workers. It is made up of a series of concise articles and monographs that thoroughly cover the progress in diagnostic roentgenology from 1952 through 1956, with the bibliography including papers through 1957. Most of the volume is devoted to articles on the use of contrast substances, particularly the various forms of angiography. Many other subjects are discussed. The short chapter on evaluation of cardiac function in the adult by roentgenographic means and the chapter on direct and differential diagnosis of diseases of the pulmonary stroma are outstanding. All of the sections are as thorough and informative as is consistent with the space available. This volume is a worthy addition to the reference textbooks on diagnostic roentgenology and, in its own right, should prove valuable. For those fortunate owners of "Roentgen Diagnostics" it is almost a necessity, as it expands and supplements that work to perfection. The editors, authors, and translators have, as before, done a fine job. It is hoped that in the future the lag between translation and publication can be shortened.

The Cervical Syndrome. By Ruth Jackson, B.A., M.D., F.A.C.S., Clinical Assistant Professor of Orthopaedic Surgery, University of Texas, Southwestern Medical School, Dallas. Publication number 334, American Lecture Series, monograph in Bannerstone Division of American Lectures in Orthopaedic Surgery. Edited by Charles Weer Goff, M.D., Associate Clinical Professor of Orthopaedic Surgery and Lecturer in Anatomy, Yale University School of Medicine, New Haven, Conn. Second edition. Cloth. $6.50. Pp. 197, with 90 illustrations. Charles C Thomas, Publisher, 301-327 E. Lawrence Ave., Springfield, Ill.; Blackwell Scientific Publications, Ltd., 24-25 Broad St., Oxford, England; Ryerson Press, 299 Queen St., W., Toronto 2B, Canada, 1958.

This book describes and differentiates between the pathological conditions in the cervical spine which may produce headache and pain or stiffness of the neck and shoulder. The structure and the lesions of the cervical spine, with particular reference to the posterior-lateral facets described first by Von Luschka, are graphically described and illustrated. The mechanism and significance of the whiplash injury are thoroughly discussed. There are 40 new illustrations, including colored drawings of the anatomy of the cervical spine. This valuable book should be useful to the general practitioner, orthopedist, and neurosurgeon.

Ophthalmic Plastic Surgery. By Sidney A. Fox, M.S. (Ophth.), M.D., F.A.C.S., Associate Clinical Professor of Ophthalmology, New York University Post-Graduate Medical School, New York. Second edition. Cloth. $15. Pp. 324, with 149 illustrations. Grune & Stratton, Inc., 381 Fourth Ave., New York 16; 99 Great Russell St., London, W. C. 1, England, 1958.

This edition, appearing five years after the first, emphasizes pictures and illustrations rather than written explanations. The drawings are simple and clear. Only that part of the anatomy of the brow

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and lids that pertains to plastic surgery is included. One of the highlights of the book is the chapter on ptosis, in which the author does not outline innumerable procedures to confuse the reader but carefully depicts a few procedures of each type in detail with some modifications of his own. In other words, this is not an encyclopedia but an ophthalmic plastic surgery book based on surgical procedures performed by the author personally. Because of the tremendous increase in traumatic accidents involving the face and eyes, this book assumes increasing importance in ophthalmic practice. It behooves all ophthalmic surgeons to familiarize themselves with its contents.

Electrocardiography. By Michael Bernreiter, M.D., F.A.C.P., Assistant Clinical Professor of Medicine, University of Kansas Medical School, Kansas City. Cloth. $5. Pp. 134, with 92 illustrations. J. B. Lippincott Company, 227-231 S. Sixth St., Philadelphia 5; 4865 Western Ave., Montreal, Canada; Pitman Medical Publishing Company, Ltd., 45 New Oxford St., London, W. C. 1, England, 1958.

This book was designed for the beginning student in electrocardiography. Its purpose is to clarify the basic principles involved in the study of electrocardiograms and their clinical interpretation. The author has done a commendable job in explaining the physiology and electrophysics in both normal and abnormal electrocardiograms by liberal use of schematic illustrations. After establishing the foundation of the electrical phenomena of electrocardiography, their clinical application is discussed. This has been documented with good illustrative electrocardiographic tracings. The author has covered arrhythmias, heart block, hypertrophy, currents of ischemia, and changes resulting from necrosis of the myocardium, plus the characteristic patterns of the various forms of electrolyte imbalance. Also discussed are the effects of digitalis and quinidine and the significance of alterations in the Q-T interval. The author spent much time in the planning and illustration of the material presented. He also avoided long and technical discussion of controversial phases of electrocardiography. Any reader who devotes time to this subject should be amply rewarded by being able to read competently most of the electrocardiograms he sees.

Pediatric Surgery. By Orvar Swenson, Professor of Pediatric Surgery, Tufts University School of Medicine, Boston. Foreword by William E. Ladd. Cloth. $20. Pp. 740, with 980 illustrations. Appleton-Century-Crofts, Inc., 35 W. 32nd St., New York 1, 1958.

This book is an up-to-date, easily readable, and comprehensive new work that covers essentially all aspects of pediatric surgery. Its author is an authority in the field; his work on megacolon is especially noteworthy. This book will undoubtedly be regarded as a standard textbook on this subject. The volume is beautifully illustrated with diagrams, photographs, and roentgenograms of most of the subjects covered. There are, in addition, numerous tables, formulas, and charts covering most aspects of pediatric surgical care. Most of the discussions include anatomic and diagnostic considerations and details of preoperative care, anesthesia, operative technique, postoperative management, and effectiveness of the management. The details of a number of relatively minor surgical manipulations, such as bronchoscopy, cystoscopy, insertion of a chest tube, and sigmoidoscopy, are aspects of this book especially valuable for the intern or resident. The operative techniques of the larger procedures are also presented in step-wise fashion and, again, with excellent illustrations. The chapters dealing with megacolon and with urologic problems are especially well written. Chapters on the management of congenital malformations of the head and neck, burns, fractures, and surgical lesions of the skin and extremities are also presented. A relatively new clinical entity, chalasia, is also discussed. This book should appeal as much to the undergraduate student of medicine as to the intern, resident, and surgeon.

The Care of the Patient in Surgery Including Techniques. By Edythe Louise Alexander, R.N., B.S., M.A., Director of Nursing Service and Principal of School of Nursing, Lutheran Medical Center, Brooklyn. [Previous editions titled Operating Room Technique.] Third edition. Cloth. $12.75. Pp. 840, with 555 illustrations. C. V. Mosby Company, 3207 Washington Blvd., St. Louis 3, 1958.

It is indeed rare to visit an operating suite that does not have a copy of Alexander's now classic work. This new edition is excellent and a worthy successor to its predecessors. It is concerned primarily with operating room procedures and armamentarium. Although it is beamed to nurses, it might be of great value to the young surgeon as a general review of procedures and an orientation in the responsibilities of the operating room staff. The general format of the book has not been changed, although there has been much revision reflecting changes in surgical procedures in the past nine years. The chapter on neurosurgery is especially well written. That on cardiovascular operations considers the established procedures being performed in most hospitals today but does not discuss the highly technical procedures requiring bypass and oxygenating equipment. The author is to be complimented on writing a concise informative textbook. It can be recommended highly to all persons interested in surgery and especially to those who provide and maintain the asepsis so necessary to the success of any operation.

QUESTIONS AND ANSWERS

ASIAN INFLUENZA

To the Editor:—*How effective is the Asian influenza vaccine? In the United States in the 1957-1958 epidemic, how many persons suspected of having this disease had blood tests made to confirm the diagnosis? Of these tests, how many gave positive results?*

Victor W. Higgins, M.D., Essex, Conn.

Answer.—In the summer of 1957, as soon as influenza vaccines of desired potency became available in sufficient quantities, a number of studies were conducted to assess their effectiveness against the impending epidemic of Asian influenza. The results of some of these studies are summarized in a paper by Davenport (*Pub. Health Rep.* 73:133, 1958). The estimated effectiveness of the monovalent vaccines ranged in these series between 42% in a study by Culver and Lennette and 77% in a study by Rose and associates. The effectiveness of the vaccine in both instances was estimated by comparing the attack rates from respiratory disease between vaccinated persons and suitable control groups. The substantial difference in protection in these two studies can be explained to a large extent by the differences in the antigenic potency of the vaccines used (250 and 750 CCA units respectively). The effectiveness of the vaccine is also discussed in papers by Hilleman and co-workers (*J. A. M. A.* 166:1134-1140 [March 8] 1958) and Meiklejohn (*Am. J. Hyg.* 67:237, 1958). On a nationwide basis, no data are available regarding how many persons with suspected disease had blood tests to confirm the diagnosis during the 1957-1958 epidemic or how many of these tests gave positive results. In one study of an epidemic of Asian influenza (Carey and co-workers, *J. A. M. A.* 167:1459-1463 [July 19] 1958), serologic studies, in addition to a retrospective questionnaire survey, were carried out among 428 school children; these revealed an attack rate of 65% for subjective "flu," confirmed serologically in 87%.

EQUALIZATION OF LIMB DISCREPANCY

To the Editor:—*How can equality of leg length best be obtained when there is an 8-in. difference? A 14-year-old boy has a short leg due to trophic disturbances and loss of bone substance associated with avulsion of soft parts. A tree fell on him eight years ago. The femoral neck is in valgus, and in the subtrochanteric level there is a malunion deformity of the shaft, producing an anterolateral curvature. At this same level there was loss of musculature, with the result that the bone is not normally buried in the soft tissue. This area might prove to be vulnerable to irritation from any prosthetic device which might be applied to the thigh. Most of the shortening is from lack of femoral growth, but the tibia has also failed to grow normally. On the affected leg, the knee is at about the level of the junction of middle and lower thirds of the normal thigh. The boy has no pain. By the use of a high cork lift, a pelvic tilt, and a short leg limp, the patient walks without brace, crutch, or cane but with an objectionable gait. Could any prosthetic device be applied without amputation?*

Robert C. Keys, M.D., South Norwalk, Conn.

Answer.—Eight inches of limb discrepancy, if not accounted for by loss of bone substance, probably is due to premature closure of growth of the major epiphysial disks in the knee. This may occur directly from trauma or secondarily from prolonged disability of the limb. The deformity at the hip may account for some of the apparent shortening of the limb. The femoral neck is described as being in valgus. In view of the lateral bowing deformity in the subtrochanteric region, it would seem more likely that the neck is in marked varus. If such is the case, its correction by subtrochanteric osteotomy may be of value in reducing the limp and in giving some functional lengthening of the limb. No statement is made as to the condition of the skin covering the traumatized region. It may be that some plastic procedure on the soft parts would be advisable. Roentgenograms of the knee region should be made to determine if the epiphyses have closed. If they are still growing, amputation should be postponed until growth is completed. If the true shortening of the limb amounts to 8 in., equalization of the limbs by surgical lengthening and short-

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ening of the opposite side should not be attempted. The discrepancy in length will have to be made up by some sort of prosthesis. Commonly used is an elevated platform shoe, but this is awkward and cosmetically unsatisfactory. A prosthetic device which laces on to the lower leg and contains an elevation which permits the use of the foot in marked equinus might be of service, but it, too, is cumbersome. Amputation may be most satisfactory from a cosmetic and functional standpoint; amputation above the knee may be desirable because of the great discrepancy in the level of the knee joints. This would give a thigh stump with a mechanical knee at the same level as on the normal side. Cosmetically it would be very satisfactory. Amputation below the knee would preserve the normal knee joint, but the prosthesis would have to make up for the length discrepancy and might be awkward in use. An end-bearing stump, such as with the Syme's amputation could be constructed and fitted satisfactorily. The prosthesis would encompass the lower leg, and equalization of the leg would have to be obtained by extension of the prosthesis. Cosmetically this would not be too satisfactory and, since it is not a standard limb, would be costly in its replacement over the years. Thus, any existing deformity should be corrected and any required soft parts plastic procedure done, and decision as to amputation and prosthesis should be made in consultation with a large amputation service where the experience of a limb manufacturer and a surgeon can be correlated.

CEREBRAL ANEURYSM IN CHILDREN

To the Editor:—*In children with ruptured cerebral aneurysm near the circle of Willis, what are the chances of recurrence of the bleeding in later life if ligation or obliteration cannot be carried out? Is it considered necessary to limit a child's activities for an indefinite period? For how long a time should the child be at bed rest after an attack?*

Ruskin King, M.D., Savannah, Ga.

Answer.—The fate of an aneurysm is difficult to predict because there are so many variables. Generally, the aneurysm does not give rise to symptoms until puberty or early adult life. Since the congenital defect is a weakness of the blood vessel wall, eventually, in a large percentage, it will rupture. Each episode of subarachnoid hemorrhage sharply increases the mortality. Therefore, all measures to preserve life and to diagnose and treat the aneurysm should be attempted. After the onset of the hemorrhage, the patient should remain in bed until such symptoms as headaches and nuchal rigidity disappear. The period of time is generally a minimum of four weeks. Cerebral angiography is an invaluable diagnostic method which is well tolerated by children. If the aneurysm cannot be ligated or trapped surgically, the child should be allowed to follow an essentially normal pattern of life, with the exception of limitation of physical exertion.

VAGINAL REPAIR AND CESAREAN SECTION

To the Editor:—*Does vaginal repair warrant a cesarean section in subsequent pregnancies?*

Nerio W. Pioppi, M.D., Southbridge, Mass.

Answer.—An answer to this question with an unqualified "yes" or "no" would be an incomplete one. The extensive Fothergill type of vaginal repair operation was predicated with the probability that subsequent vaginal delivery would be routine. Certainly every obstetrician can recall an instance in which delivery with hysterectomy was deemed advisable. For example, one patient had a successful closure of a vesicovaginal fistula after two previous attempts had failed. An orthodox anterior and posterior colporrhaphy seldom warrants cesarean section in subsequent pregnancies.

BLOOD EXAMINATIONS WITH OXALATED BLOOD

To the Editor:—*The answer given on the question about blood examinations with oxalated blood, which appeared in* The Journal, *Nov. 15, 1958, page 1593, is somewhat at variance with statements made by other authorities in the field. The questioner indicated that an oxalate mixture was used as the anticoagulant in a vacuum tube. The two major suppliers of vacuum tubes supply only one oxalate mixture, and that is a combination of ammonium and potassium oxalate. Wintrobe (Clinical Hematology, ed. 4, Philadelphia, Lea & Febiger, 1956, chap. 8) states, "We have found a mixture of dry ammonium and potassium oxalate to be very satisfactory." In the same chapter, he states, "It has been repeatedly shown that there is no difference in counts made on venous blood as compared with capillary blood, if proper precautions to secure a freely flowing sample are observed in each instance." Although none of the hospitals with which I am associated use vacuum tubes, I know of several reputable hospital laboratories that routinely use these, with balanced or double oxalate as the anticoagulate, for hematological procedures and find them quite satisfactory. The oxalate does alter the morphology of the leukocytes in the stained smears.*

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